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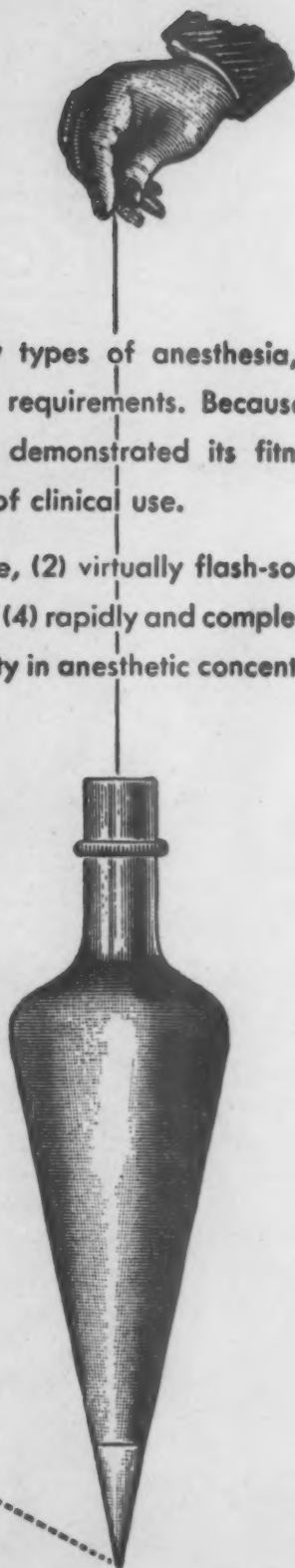
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HYPOTHERMIA

ITS POSSIBLE ROLE IN CARDIAC SURGERY:

AN INVESTIGATION OF FACTORS GOVERNING SURVIVAL IN DOGS
AT LOW BODY TEMPERATURES*

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THE USE OF HYPOTHERMIA as a form of anesthetic could conceivably extend the scope of surgery in many new directions. A state in which the body temperature is lowered and the oxygen requirements of tissues are reduced to a small fraction of normal would allow exclusion of organs from the circulation for prolonged periods. Such a technic might permit surgeons to operate upon the "bloodless heart" without recourse to extra corporal pumps, and perhaps allow transplantation of organs.

At the present time, pericardectomy as well as operations designed to revascularize^{1, 2, 3} or repair⁴ the myocardium are in the process of development; these involve the heart wall. Most so-called heart operations, however, are restricted to the anastomosis of vessels about the heart, the most notable in this category being the current operations for congenital heart disease^{5, 6} and a shunt⁷ for mitral stenosis. Intracardiac procedures upon human beings are heroic technics designed to open a stenosed mitral valve and close¹¹ or produce¹² a septal defect in an intact heart with little or no visual control. All these procedures represent advances in our knowledge, but the human heart until now has resisted serious inroads by the surgeon. The shunt operations produce a secondary, although less serious, defect and intracardiac operations under direct vision are still not possible.

A bloodless heart excluded from the circulation is necessary before much further progress can be made in the field of cardiac surgery. Methods to short circuit the heart by an extra corporal heart-lung pump have been under experimental study in different centers¹³⁻¹⁶ for several years. We have used

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hypothermia on the theory that it might prove a simple procedure allowing operations on a diseased or abnormal heart where cannulae in great vessels may be poorly tolerated. A few published reports have been encouraging as to the practical future of this study. Body temperatures as low as 25°C in human beings have been recorded¹⁷ with survival. Temple Fay¹⁸ was able to maintain the body temperature of patients under treatment for cancer at 31°C for several days.

In order to test this hypothesis, generalized hypothermia has been studied by the authors* for two years. One hundred and twenty dogs have been cooled and re-warmed. The steady fall in oxygen consumption produced by lowering body temperature has already been reported.¹⁹ The present investigation of the circulatory changes and cause of death was carried out to make possible cooling to lower temperature levels. The technic of cooling and re-warming has been developed far enough to permit the exclusion of the heart from the circulation by clamping off the vena cavae, with ultimate survival, for much longer periods than has been possible at normal body temperatures.²⁰ During the clamp off the heart has been opened then re-sutured. A report of these experiments will be published in the near future. This procedure is not yet ready for clinical trial, but it appeared worthwhile to report to others interested in this field the difficulties that have been encountered and problems that remain to be solved.

Warm blooded animals at rest have a relatively constant body temperature and display only minor variations in their cardiovascular state. When their body temperature is lowered, however, dramatic changes are observed.

Mature non-hibernating mammals such as the dog will survive cooling under certain conditions down to about 20°C. Differences of opinion exist in the literature as to the cause of death. It appears controversial whether death is due to circulatory or respiratory failure. Artificial respiration and light anesthesia were used in the experiments to be described, making it possible to study what appeared to be a cardiovascular death at temperature usually below 20°C. Interest in such an investigation is stimulated by the knowledge that hibernating mammals with similar normal anatomy can survive temperatures of 3°C.²¹ and, unlike dogs, experience little or no shivering during cooling.

METHODS

Mongrel dogs of medium size, after fasting for 20 hours, were close clipped and cooled by either of two methods. In the early experiments animals were placed in a controlled temperature room at an arbitrary temperature level of six to 12°C. Later, blankets† were used through which an alcohol solution at 1°C was circulated in coiled rubber tubing. Both methods produced a similar rate of cooling.

Barbiturates, ethyl ether and vinyl ether have been used as anesthetics to

* As well as by R. C. Harrison, M.D., and R. A. Gordon, M.D., University of Toronto.

† Refrigeration unit supplied by Therm-O-rite Products Corp., Buffalo, N. Y.

determine their relative effects on the cardiovascular system. In each case the smallest amount of the anesthetic agent required to control shivering was employed.

The animals were revived by submerging them to the neck in a hot water bath at 40° to 42°C.

The pulse rate was counted intermittently from the continuous visual electrocardiograph image,* or was obtained by measurement from the electrocardiograph photographic tracings, taken periodically.

Mean arterial pressures were read intermittently from a mercury manometer connected to an arterial catheter which had been inserted through the femoral artery into the aorta.

Mean venous pressures were obtained from a saline manometer connected to a catheter, which had been passed down the right, or occasionally the left, external jugular vein into the superior vena cava. During cooling, zero point of the manometer was set at the level of the dog's midsternum, the dog lying on its side. During re-warming in a water bath the manometer zero point was set on a level with the suprasternal notch. The lowest point of the venous pulse wave was recorded periodically. Either the manometer system or the animals were heparinized.

Cardiac outputs were calculated by the direct Fick principle.²² Oxygen consumption was measured by a 1 liter modified Tissot spirometer connected through a carbon dioxide absorber to an airtight endotracheal catheter. Samples of arterial blood were taken from the abdominal aortic catheter simultaneously with venous blood samples from the right auricle. The position of catheter was checked radiologically. The blood was collected under oil and analyses were carried out on the manometric Van Slyke apparatus.²³

During the process of cooling and rewarming, continuous visual observations and periodic photographic recordings were made on a cathode ray electrocardiograph. Leads I, II and III of the electrocardiograph were connected to German silver needle electrodes which were placed sub-cutaneously on the proper limbs. Arterial blood samples for the determination of serum calcium and potassium were obtained in an oiled syringe through a large bore cannula lying in the aorta. They were centrifuged in a waxed tube. As soon as the clot formed the serum was removed as rapidly as possible. Calcium was determined by the method of Collip and Clark as modified by Fiske and again by C. E. Downs.²⁴ Potassium was determined as by Consolazio and Talbott.²⁵

When respirations failed at lower temperatures positive pressure artificial respiration was used. The lungs were inflated with a 5 per cent carbon dioxide in 95 per cent oxygen mixture ten times a minute.

OBSERVATIONS

The general picture of a dog undergoing cooling and re-warming, together

* "Cathode Ray Electrocardiograph"; supplied by Smith and Stone, Georgetown, Ontario.

with the methods of maintaining arterial oxygen saturation have been described in a previous publication. With proper control of shivering, each dog showed a progressive fall in body temperature and respiratory rate. When the rectal temperature had fallen to 28°C "cold narcosis" supervened, anesthetic agent was no longer necessary to maintain relaxation, and a little later spontaneous respirations ceased. In this state the animals were ideally suited for surgical procedures. The rate of re-warming was faster than the rate of cooling, and spontaneous respirations reappeared at 22° to 27°C. These animals, after seven hours of unconsciousness, were usually up and active two to eight hours

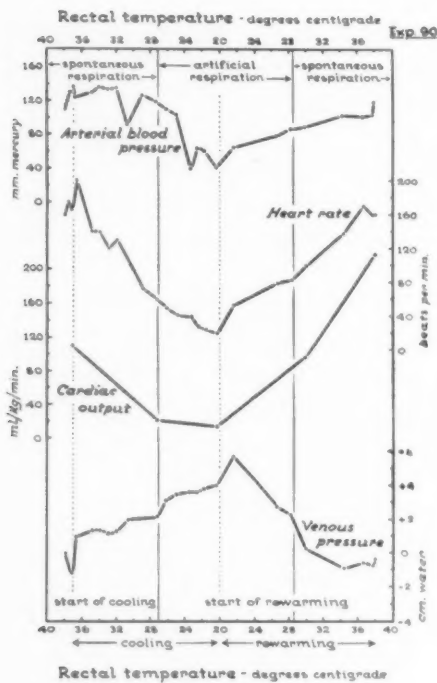


FIG. 1

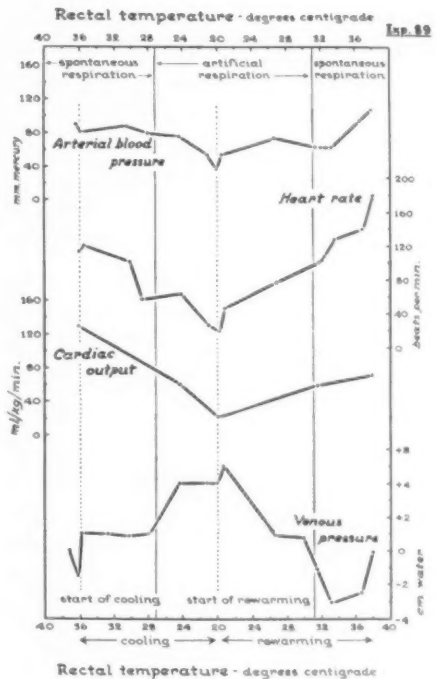


FIG. 2

FIGS. 1. and 2.—Observations made while cooling a dog to 20°C with re-warming in a water bath at 40°C.

after resuming normal body temperature. Absence of ill effects on examination up to seven months after cooling has been reported.¹⁹ Repeated cooling did not appear harmful.

No attempt has been made to obtain a survival rate in a large group of dogs cooled to a given temperature level such as 20°C with immediate re-warming. In many experiments cooling was continued to the lowest possible limit in order to determine the lethal temperature level. We feel, however, that cooling dogs to 20° with re-warming is a safe procedure.

HYPOTHERMIA

Three separate series of animals were studied under different forms of anesthesia. The largest and most complete studies were made on animals under barbiturates. This report is based largely on this series.

HEART RATE

The heart rate was observed in 72 dogs during cooling to levels usually between 18° to 22°C . The 59 dogs under barbiturate anesthesia are reported in this section. All animals showed a decrease in rate from a normal of 120 to 180 per minute as their body temperature fell, agreeing with other observers,²⁰⁻³² and observers not herein cited. An initial transient rise of ten to 15 points in heart rate on first exposure to cold, reported by many of these workers, was observed in the majority of animals; its appearance was noted in those which were more lightly anesthetized. This initial rise was eliminated by deeper anesthesia, under which conditions a steady fall in rate was observed.

Although for each animal a linear relationship was found during cooling between the curves of body temperature and of heart rate there was some variation in the slopes of the heart rate curves because of the initial differences in the normal rates of these dogs. The final rate of temperatures between 18° and 20°C was fairly uniform, the range for the whole group being from 15 to 30 beats per minute (see Figures 1, 2 and 3).

During re-warming there was a rapid increase in heart rate immediately after immersion in the water bath at 40°C . From this point the rate rose with increasing body temperature, parallel to the fall during cooling, although at a given temperature the re-warming heart rate was usually faster. Failure of the heart rate to increase on re-warming was an indication of a reduction in the animal's chances of late survival. A similar variation in the slopes of the re-warming graphs to that noted in cooling was observed.

ARTERIAL PRESSURE

Mean arterial pressures have been studied on 18 dogs during cooling. Six experiments under barbiturate with three of these during re-warming are

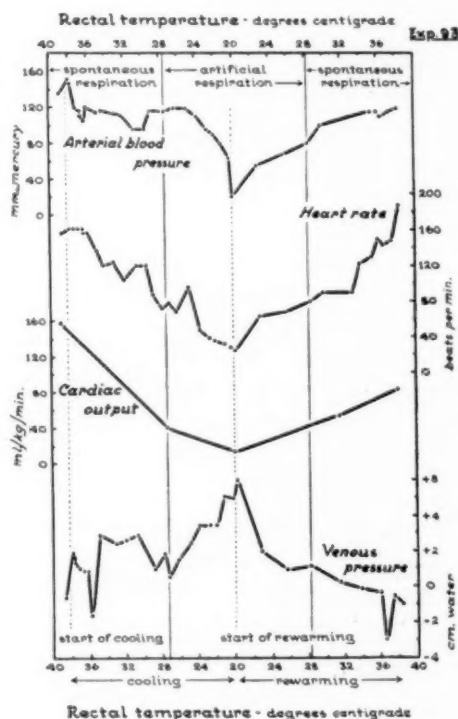


FIG. 3.—Observations made while cooling a dog to 20°C with re-warming in a water bath at 40°C .

reported. Cooling in dogs has been shown by Prec *et al.*³¹ to lower blood pressure, but in a relatively constant manner. In our animals, cooling lowered the blood pressure, but in a variable manner.

In four of the dogs a rise in pressure occurred shortly after being placed in the cold environment, a finding in agreement with other observers.^{26, 28-31, 33} Readings are not available on the other two dogs for the first few minutes of cooling; they may or may not have shown initial rises. The early arterial pressure rise was followed by a fall before the animal had cooled more than 2°C. The pressure tended to become stabilized or to rise slightly again, between 32° and 24°C, in all dogs. This trend has not been remarked upon by other workers. Following this short period of stabilization the blood pressure fell off rather sharply, usually in the temperature zone of 24° to 20°C. A mean blood pressure of 16 to 46 mm Hg. was recorded for all six dogs at 20°C. The pressure never fell to zero unless the heart became irregular or stopped (see Figures 1, 2, 3).

VENOUS PRESSURE

Venous pressures have been studied in 27 dogs during cooling and re-warming. Twelve experiments under barbiturate are reported in this section. This study was prompted by the observation in early experiments that in some of the dogs undergoing cooling in the lower temperature a marked dilatation of their superficial veins became apparent. This observation has been made on animals by several authors. Alexander³⁴ reports similar observations having been made on human beings by German investigators in Nazi prison camps.

The pressures in the superior vena cava or the right auricle before cooling were -1.5 to +2.2 cm. of water. There was a fall of one to three cm. in the venous pressure of two thirds of the animals shortly after being placed in the cold blankets. During further cooling there was no consistent or significant change in pressure while good spontaneous respirations were maintained. Usually positive pressure artificial respiration was started at about 27°C. This was followed by an immediate rise of 1 to 3.5 cm. in venous pressure. From that point until 18° to 22°C, when re-warming was started, there was a further gradual rise in pressure. Pressures up to 20 cm. of water have been recorded.

As a rule venous pressures over 6 cm. of water maintained for any length of time were followed by abnormal heart action, from which the dogs seldom recovered in the earlier experiments. There were no records of a negative venous pressure at a body temperature below 22°C.

During resuscitation there was a further rise in venous pressure shortly after immersion in the water bath (40°C), sometimes followed by ventricular fibrillation and death. If the animal experienced the sudden increase in heart rate usually following immersion in warm water, the pressure rise was only temporary, and soon fell to within normal limits. A further fall in pressure to a negative range occurred with the onset of spontaneous respirations.

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It was apparent that a full understanding of venous pressure changes might well hold the key to a more exact knowledge of cardiovascular failure associated with hypothermia. With this in mind an appraisal of factors affecting venous pressure changes was made.

There were occasional transient periods of shivering during cooling in a few animals in this series. Moderate to severe shivering was associated with an increase in venous pressure, but the pressure returned to normal when the shivering was controlled by further anesthetic. Crismon, who did not control shivering in rats, reported a consistent and marked rise in venous pressure during cooling which eventually decreased with cessation of shivering.

There were no records of negative venous pressure after the animal had been on positive pressure artificial respiration for any length of time. In two young dogs in which spontaneous respirations were maintained to 22°C and 24°C a corresponding delay in rise of venous pressure occurred.

As a general rule the greater the depression of heart rate, the greater was the tendency to develop increasing venous pressure as cooling proceeded.

VENESECTION

It has been observed incidentally that drawing off blood samples at very low temperatures increased the heart rate. With the observed correlation between a rising venous pressure and the onset of ventricular fibrillation, the obvious procedure to investigate was the effect of venesection.

Previous to this, 17 experiments had been terminated prematurely by a "cardiac crisis" with the sudden onset of ventricular fibrillation in 15 and cardiac arrest in two as observed in the continuous electrocardiographic image. Fifteen of the 17 animals died without resuming normal heart action (including the two with cardiac arrest). This was so in spite of immediate immersion of most of the animals in the water bath within one to two minutes of the development of fibrillation.

Venesection has been performed 60 times. The first experiment was dramatic in its result. At 19°C and with a venous pressure of 7.5 cm. of water, ventricular fibrillation appeared and the dog was immediately placed in the warm bath. Four minutes later, on removing 30 cc. of blood from the jugular vein, a run of normal beats was produced. Removal of a further 100 cc. established normal heart action and the dog survived. Venesection was successful in 20 out of 28 instances in which it was used in an attempt to restore normal heart action after "cardiac crisis" in dogs cooled below 21°C. This sequence of events has occurred two or three times in the same experiment during cooling and re-warming with survival of the animal. On six occasions the measure had no effect and twice it converted ventricular fibrillation into complete A-V block with independent action of auricles and ventricles. Amounts withdrawn varied between 30 and 150 cc. and averaged 80 cc.

The procedure was used 32 times as a means of reducing a venous pressure which had become dangerously high. By an average withdrawal of 80 cc. the

pressure was reduced an average of 2.0 cm. water. On one occasion no fall in venous pressure followed venesection.

In three experiments an attempt was made to keep the venous pressure normal during cooling by repeated small venesections of 50 cc. of blood as required. After each withdrawal the venous pressure was lowered, the heart rate increased and ST interval in the electrocardiogram shortened. The animals were cooled to lower levels than that usually attained, but in each case two thirds to three fourths of their total blood volume was eventually removed with final "cardiac crisis" and death.

CARDIAC OUTPUT AND PERIPHERAL RESISTANCE

The cardiac output was measured at intervals during cooling and re-warming in seven dogs making use of the Fick principle.²² The results in three dogs are shown in Figures 1, 2 and 3. A gradual fall during cooling and a rise during re-warming is evident with a cardiac output averaging 18.1 ml./Kg./

TABLE I.—*Index of Peripheral Resistance During Cooling and Re-Warming.*

Experiment Number	Rectal Temperature	Index Periph. Resistance
93	38.0	9
	27.3	20
	20.0	12
	31.7	20
	38.0	16
90	37.2	9
	27.2	40
	20.3	20
	30.0	7
	37.2	6
89	36.1	7
	24.4	12
	20	15
	31.1	9
	38	13

min. at 20°C. This represented a fall to 14 per cent of the average of the pre-cooling figures.

Final re-warming values were below the pre-cooling in all but one. In this experiment the observations are made one hour after normal body temperature had been reached and the animal had been removed from the warm bath.

Peripheral resistance was assessed by applying the formula $R = P/F$ (peripheral resistance = blood pressure/cardiac output). Without discussing the reliability of this formula the results are given in Table I. These calculations are from the experiments represented in Figures 1, 2 and 3.

The marked rise in the index of peripheral resistance is evident in each of the three dogs examined.

THE PERIPHERAL VASCULAR BED

As cooling progresses the peripheral vessels undergo a gradually increasing vasoconstriction. No attempt has been made to measure the degree or rate of this process, but the femoral and subclavian artery and vein have been

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exposed on numerous occasions and at various temperature levels. At 20°C. it is practically impossible to do a venous or arterial puncture through the skin, and on exposure the vessels appear constricted to less than one-half diameter, although blood flow continues.

Microscopic examination of the conjunctival vessels before and during cooling (using a technic previously described⁸⁵) revealed the development of marked "vascular stasis" in the lower temperature ranges, with complete

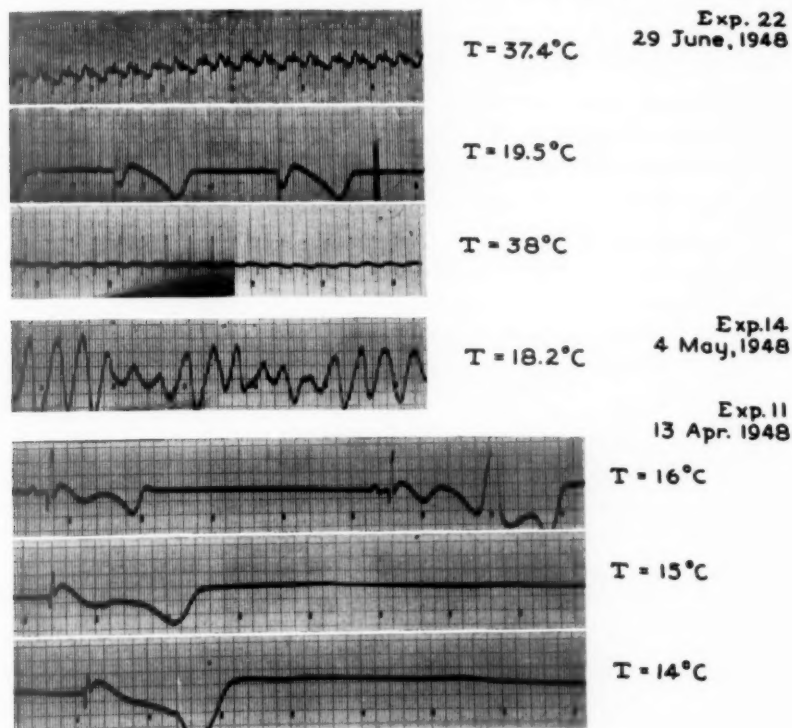


FIG. 4.—A group of representative electrocardiograms at low temperature. —(1, 2 and 3) The changes in the electrocardiogram on cooling and re-warming. The standardization in (2) and (3) is half that in (1) since it was impossible to photograph the whole complex with normal standardization at low temperature. (4) Ventricular fibrillation in a dog at low temperature. (5) Slow sinus rhythm with a ventricular premature beat. (6) Slow A-V nodal rhythm at 15°C. Interval between beats 8 to 12 seconds. (7) The same at 14°C. Intervals between beats is about 14 seconds.

cessation of flow in some arterioles and in veins as large as 60 microns in diameter. This effect was considered due to obstruction to flow caused by the "intravascular agglutination of erythrocytes" (sludged blood) along with vasospasm.

CHANGES IN THE ELECTROCARDIOGRAM WITH COOLING

Representative electrocardiograms in cooled dogs are shown in Figure 4. The continuous electrocardiographic image has been followed during cooling

and re-warming in 95 animals. Tracings at various temperature levels have been taken and studied on 15 representative experiments. During cooling the rate slows, sinus rhythms with rates of 15 to 30 per minute being usual at 20°C. The PR interval is roughly twice the PR interval at 37°. The duration of the QRS becomes difficult to define at temperatures below about 25°C. The initial rapid deflections are succeeded by a long wavy electrical disturbance. The initial rapid deflections are called the QRS, even though it is sometimes hard to decide whether part of the subsequent disturbance rightly belongs to the QRS. The subsequent electrical disturbance, which lasts until the diastolic isoelectric line is reached, is considered to be the T wave. Around 20°C it is nearly always a negative wave. It may become negative at any stage of cooling, and the earlier it appears the poorer the prognosis. The duration of the QRS is usually about doubled, and the QT interval (electrical systole) is three to four times as long as at 37 degrees. This can be seen by a glance

at Table II.

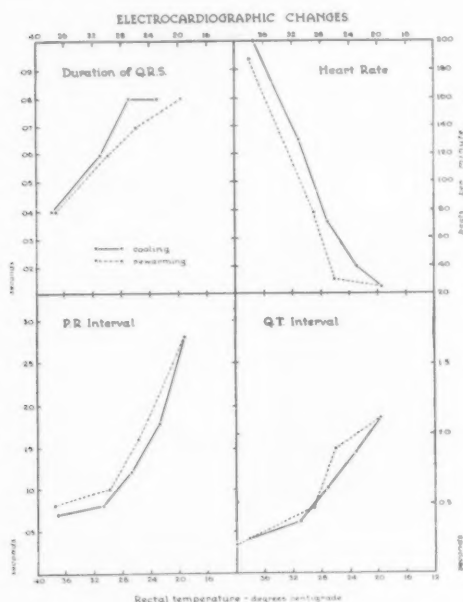


FIG. 5.—The changes in certain of the electrocardiographic measurements with cooling and re-warming in a representative dog. Dotted line is re-warming.

of change is variable. The most common sequence of events is the appearance of ventricular ectopic beats followed by ventricular fibrillation and death. There

The voltage of the QRS is difficult to measure in the dog, since the deflection is often so great and rapid that it does not photograph, even though it may be visible on the cathode ray screen. It can be photographed by lowering the sensitivity of the instrument. About 24°C the voltage may fluctuate, more often it increases. Below 24° the voltage usually falls, but this is not constant; it was observed in five out of seven dogs in which it was possible to measure the QRS voltage in our records. Figure 5 shows that the PR and QT distance increases much more rapidly with falling body temperature, once 30°C is passed. If cooling is continued the rhythm changes at some point, usually below 20°C and above 16°C. The type

TABLE II.—Changes in the Electrocardiogram at Low Body Temperature (Nine dogs).

Rectal Temp. °C.	36.8°C (32° to 39°)	19.3°C (18.7° to 20°C)
	(before cooling)	
Heart rate.....	143 (100 to 200) per min.	25 (20 to 30) per min.
PR interval.....	0.10 (0.07 to 0.12) sec.	0.22 (0.16 to 0.28) sec.
QRS duration.....	0.05 (0.04 to 0.06) sec.	0.07 (0.07 to 0.12) sec.
QT interval.....	0.25 (0.18 to 0.36) sec.	1.04 (0.92 to 1.14) sec.

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is usually little warning. With vigorous ventricular fibrillation it is impossible to identify P waves. Direct observation of the heart, however, discloses that there is a continuance of regular auricular beats for periods up to 20 minutes after onset of ventricular fibrillation. These become irregular and eventually both auricle and ventricle come to cardiac arrest in diastole.

On rare occasions, and usually below temperature levels of 17°C , instead of ventricular fibrillation, a pacemaker in or below the AV node has taken over, resulting in the electrocardiographic appearance of nodal rhythm, or of slow idioventricular rhythm. The interval between beats may be as long as 17 seconds, with absence of P waves.

Survival after ventricular fibrillation has been described under the section on venesection.

If the animal is re-warmed, the changes in the electrocardiogram revert toward normal (Figure 5). However, even though the heart rate, the PR interval, the duration of the QRS complex and the QT interval return to normal, the voltage of the QRS is often lower than before cooling, and the T waves and the ST segments may be of a different form. Records taken on a series of six animals one to three months after cooling showed normal tracings. These changes in the electrocardiogram with cold are not unlike those reported by other observers.²⁸⁻³¹

DIRECT INSPECTION OF THE HEART AND CARDIAC RESUSCITATION AT LOW BODY TEMPERATURES

Thoracotomy has been performed upon 20 dogs at low body temperatures ranging from 15°C to 22°C , no anesthetic agent being required. The heart has been observed directly with its normal slow beat and as changes in rhythm occurred. Several methods of cardiac resuscitation have been employed.

At these temperatures a state of almost pure cold narcosis exists as an anesthetic, two hours having usually elapsed since removal of the anesthetic agent.

Interesting slow heart action was observed. As the venous pressure increased, overfilling and distention of the right auricle was noted during diastole with a slow but powerful contraction occurring only a few times a minute. It is an intriguing sight resembling a slow motion movie recording of heart action. Ventricular fibrillation appeared at low temperatures with little warning and was characterized by a slow irregular writhing of the ventricular musculature. Usually the auricle continued a regular beat following the onset of ventricular fibrillation but, as a rule, for not more than 15 to 20 minutes. Isolated, irregular auricular beats often continued for an hour with a reduction in vigor of the ventricular fibrillation and eventual cardiac arrest in diastole.

Cardiac resuscitation has been employed in the form of: (1) electrical stimulation with a faradic current, (2) mechanical prodding, and (3) manual cardiac massage. Normal beats with auricular and ventricular com-

plexes have been produced by stimulation of the SA node area in the right auricle with the heart in both ventricular fibrillation and following cardiac arrest. Electrical stimulation in such cases was of low voltage from an induction coil. After a period of about 15 minutes only the auricle will respond to this stimulation. Solitary ventricular contractions may sometimes be obtained by similarly stimulating the ventricular muscles for a further period of about 15 minutes. Epinephrine, barium chloride, digitalis and Coramine have all been used as an intracardiac injection without significant response. A strong electric shock was applied to three hearts while in ventricular fibrillation according to the defibrillation technic described by Beck.³⁶ One of these hearts immediately developed cardiac arrest, the others were unaffected.

No cases of ventricular fibrillation or cardiac arrest were permanently revived by these methods alone. Rapid removal of venous blood, which reduced or eliminated the ventricular fibrillation, followed by cardiac massage and re-warming, did allow revival of a few.

TABLE III.—Serum Calcium and Potassium Changes in Hypothermia
(*Seconal anesthesia*).

Experiment	Serum Calcium Mg. %		Serum Potassium Mg. %	
	Pre-cooling 36–37.5°C.	Hypothermic 19.5–21.5°C.	Pre-cooling 36–37.5°C.	Hypothermic 19.5–21.5°C.
XXVI.....	10.0	12.80
XXVII.....	12.20	12.80
XXXII.....	9.96	14.86
XXXIII.....	9.94	17.40
XXVIII.....	11.30	14.43	14.82
XXI.....	15.02	12.40	10.95	13.30
XXIX.....	12.0	16.0	10.92	12.87
XC.....	10.60	11.40	14.46	16.81
XCIV.....	10.20	11.20	14.14	16.21

SERUM CALCIUM AND POTASSIUM CHANGES

This investigation was carried out to determine whether there were electrolytic changes which might account for the cardiovascular collapse encountered in cooling at low temperatures.

Using barbiturate anesthesia and methods previously described, estimations were made before cooling and again in the temperature zone of 19° to 21°C. The enclosed table illustrates a constant rise in serum potassium with a variable effect upon serum calcium. This is for the most part similar to the results obtained by Elliott and Crismon,³⁷ who, however, noted a consistent rise in both calcium and potassium level in rats.

EFFECTS OF ANESTHETICS

Two further series of dogs have been studied, using different types of anesthetic agents. Cardiovascular changes observed were compared to the barbiturate series just described.

Series II: Vinyl Ether. This is a very rapidly acting form of inhalation anesthesia. As in the barbiturate series, just sufficient was administered to

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control shivering. The blood pressure, heart rate, respiration, venous pressure and electrocardiogram were recorded on five dogs.

During cooling, their general condition appeared better than the dogs under barbiturate. There was improved heart action, slightly faster heart rate, and better respiration. Spontaneous respiration ceased on an average at 22°C. and reappeared at 23°C. The venous pressures were maintained at a lower level.

It was a surprise to find that only one of the five dogs survived the experiment. This dog died four days later with signs of clinical jaundice and Vandenberg estimation in the blood of 7 units. The other four died during re-warming and all showed congested livers at autopsy.

Series III: Ethyl Ether. Thirteen dogs were studied in this series. The heart rate was followed in all. The venous pressure was recorded in ten, the arterial pressure in four. There was no significant difference in the readings obtained in this group compared with those under barbiturate anesthesia. The heart showed the same tendency to develop abnormal action at low temperature.

DISCUSSION

Most workers have accepted shivering as a part of the physiologic response to cold, observing its variability during the early stages of cooling and its gradual decline as cooling proceeds. They have made their experimental observations in the presence of shivering. In these studies in hypothermia, shivering has been controlled in order to study the pure effects of cold on the organism. This method of approach was used in a previous study of oxygen consumption¹⁹ and the possible source of error introduced by the use of anesthetic was discussed. Admittedly anesthesia affects heart action and the vascular bed to some degree, but when given carefully in regulated doses the resultant absence of shivering allows ready cooling and technically more reliable observations. It is the approach to hypothermia which one would anticipate in its eventual clinical application.

Figures 1, 2 and 3 show a marked fall in cardiac rate, cardiac output and blood pressure (which is remarkable when one realizes that it is compatible with life). The low hydrostatic pressure and vascular stasis from agglutination of erythrocytes must leave the peripheral tissues almost devoid of blood flow. Since skin and muscle temperature are well below the rectal temperature¹⁹ their oxygen requirements are negligible. The whole animal at 20°C uses about 15 per cent of its normal oxygen consumption,¹⁹ which roughly corresponds to the reduction in cardiac output at that temperature level. Recently published experiments¹⁷ report clamping off the heart for periods of nine minutes at normal body temperature. We have excluded the heart from circulation for longer periods with the animal at body temperature of 20° but for the prolonged exclusion considered necessary for human cardiac surgery, lower body temperatures will likely have to be attained.

When dogs are cooled with the aid of a light anesthetic to prevent shivering, they become hypoxemic due to respiratory depression. This respiratory depression is a combined result of the anesthetic agent and cold. Artificial respiration below a certain temperature level is necessary to maintain life and it has been used in each experiment recorded. Such an experimental animal will usually survive cooling to about 20°C provided he breathes a mixture of 5 per cent carbon dioxide in oxygen.¹⁹ Below this temperature range he usually develops ventricular fibrillation, which is invariably fatal unless venous section is employed and re-warming instituted.

Under the condition of these experiments death in hypothermia appeared to be the result of sudden cessation of normal heart action (cardiac crisis). The possible causes of this may be summarized as follows:

I. Primary effect of cold on the heart

- A. Inhibition of impulse formation.
- B. Interference with function of conducting tissue.
- C. Failure of myocardium to respond.

II. Cardiac crisis secondary to:

- A. Overwork from too great a peripheral resistance, caused by intense vasospasm, induced by cold.
- B. Overwork caused by overloading, from increased venous return, due to reduction of the vascular bed by vasospasm,
- C. Anoxia of the heart.
- D. Chemical changes in the blood
 - 1. Fluid and electrolyte shifts.
 - 2. Circulating toxin.
- E. Depression of nervous system
 - 1. Central, cardiac center.
 - 2. Peripheral, autonomic nerves.

I A. Direct observation of the persistence of regular auricular beats in the presence of early ventricular fibrillation indicates the continuance of impulse formation and rules out inhibition of impulse formation as cause of death.

I B. There is evidence that in the cold heart the conducting tissues function poorly. Figure 5, showing the relation of PR interval to temperature, shows a very great increase for a small drop in temperature once 20°C is passed. Whether or not this impaired conduction is responsible for the great tendency of the cold ventricle to fibrillate and then stop is not known. The late response of the cardiac muscle to direct stimulation, in our attempts at cardiac resuscitation as described, could be due either to increased myoneural threshold or depression of the conducting mechanism.

I C. The primary effect of cold on the heart may well be a chief cause of death. It has been demonstrated that isolated heart preparations from non-

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hibernating animals cease functioning at 16°C while that of a hibernating animal continues to 2° and 3°C.³⁸

II A. The concept of a high peripheral resistance at low body temperatures producing an overworked heart is suggested by our calculation of peripheral resistance (Table I³⁹) and by the intense vasoconstriction present in the extremities. One would expect the "vascular stasis" observed microscopically to cause a great increase in peripheral resistance. Arteriovenous shunts probably open as a compensatory mechanism.³⁵

On examining the blood pressure changes during cooling, one does not see a temporary rise in blood pressure before cardiac failure which might be expected if this concept were true. However, there is a tendency for the blood pressure to remain at a relatively constant level following an initial fall until about 24°C when it usually falls rather more sharply.

II B. It was observed that an increasing or prolonged increase in venous pressure was a forerunner of ventricular fibrillation. Our initial interpretation of this was that it was a result of developing cardiac failure. However, we have recently considered the increased venous pressure as a possible cause of failure. This was first suggested by the favorable effect on heart action produced by venous section as described above. We were able to increase the rate, reduce venous pressure, and bring a heart back from ventricular fibrillation to normal by venous section.

Recent workers^{40, 41} have shown that venesection improves cardiac output while lowering the venous pressure in low-output congestive failure. Their theory that relief from overstretching in diastole allows more efficient ventricular contraction is in keeping with our observations of the effect of venesection in the cold state.

The increased venous pressure may be partly due to the generalized constriction of the vascular bed. It is definitely produced by the institution of positive pressure artificial respiration, which in itself may be a large factor in the cause of death. It was apparent that increased venous return at best is only a contributing factor to cardiac failure. Our experiments in which the venous pressure increase was prevented by repeated venous section only allowed us to cool the dogs a few degrees further.

II C. The cardiac failure in hypothermia is similar to that induced by hypoxemia, both in its course and in the electrocardiographic changes observed. One likely cause for this in the presence of full oxygen content of arterial blood would be reduced coronary flow occasioned by the low systemic blood pressure. Perhaps reduction in the availability of oxygen, caused by low body temperature,¹⁹ is sufficient to produce serious myocardial anoxia.

II D. Biochemical changes in the blood induced by cold are being studied and will be fully published later. The potassium and calcium changes may be significant factors in the mechanism of cardiac failure.

Workers who have studied the cardiac effects of changes in blood level of calcium and potassium have dealt with much greater variations than were

observed in this study. It is difficult to conceive of the change noted in these experiments being the sole cause of the dramatic electrocardiographic changes seen, although Elliott and Crismon³⁷ conclude that there is an increased sensitivity to injected potassium at low body temperatures. The statistically significant figures of these workers for potassium elevation were produced under different conditions. The rats of their experiment were shivering violently and perhaps liberating potassium from the liver.

Circulating toxin from the liver or accumulated as a result of the reduced renal output could be a factor.

II E. The mode of death does not suggest a central depression of the nervous system, although denervated heart preparations have not been studied. Chatfield⁴² has recently demonstrated that the peripheral nerves of a hibernating golden hamster did not cease functioning until an average temperature of 3° to 4°C was reached, while nerves from (non-hibernating) rats ceased functioning at an average temperature of 9°C.

Behind all this discussion of the mechanism of cardiac failure is the basic problem concerning the mode of action of hypothermia. Does cold below 20°C prevent oxygen from entering the tissues? Does it depress some phase of cell metabolism? We feel that the intact dog may never be reduced to the low temperature attained by hibernating animals without recourse to special procedures. The difference may be in the conducting mechanism of his nerves or in the anatomy of the arteriovenous shunts in the peripheral vascular bed. Other factors likely contributing to "cardiac crisis" in dogs at low body temperature are cardiac anoxia, overfilling of the heart, and electrolytic changes in the blood.

SUMMARY

1. Hypothermia was induced in dogs, with shivering controlled by anesthetic, in order to study the physiology of the cardiovascular system and learn something of the mechanism of death at low body temperatures.
2. This was investigated to improve our method of cooling with a view to excluding the heart from the circulation for longer periods.
3. Re-warming was accomplished by means of a water bath at 40°C.
4. There was a gradual fall of blood pressure, heart rate and cardiac output to very low levels as cooling progressed, with a comparable rise on re-warming.
5. Intense vasoconstriction was observed in the gross, and vascular stasis with erythrocyte agglutination observed microscopically at low body temperatures.
6. Venous pressures proved a valuable guide to the condition of the heart. An increase in venous pressure over too long a period was often followed by "cardiac crisis" and it could be temporarily forestalled by venesection.
7. Electrocardiographic studies during cooling and re-warming are summarized.

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8. Ventricular fibrillation usually caused death between 16° and 22°C.
9. Return of the heart from ventricular fibrillation to normal with revival has been accomplished by venesection and immediate re-warming. Cardiac resuscitation was attempted through a thoracotomy incision.
10. A table of the possible causes of death has been drawn up and the various factors discussed.

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THE CASE FOR BRANCHIOGENIC CANCER (MALIGNANT BRANCHIOMA)*

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"If there is one pit-fall in science more dangerous than another it is that of regarding hypotheses as proven facts."—William H. Welch.

THE THEORETICAL CLINICO-PATHOLOGIC ENTITY known as malignant branchioma is somewhat unique in the field of oncology for the reason that in the final analysis its chief distinguishing characteristics are negative rather than positive. The main basis for the belief in the existence of such an entity rests solely on the fact that offhand there is no other more reasonable explanation for the histogenesis of certain cervical tumors. In this report the evidence both for and against the existence of such a specific tumor as branchiogenic cancer will be presented and analyzed.

In 1940, when we began the review of the clinical material in preparation for this study, we held the commonly accepted view that such an entity existed, although we realized, as many others, that the diagnosis of branchiogenic cancer is too often and too loosely made. This paper has been re-written a number of times as the clinical material and the general subject has been more critically reviewed, and the longer we consider the proposition the less confidence we have in the existence of an entity which warrants the specific name "branchiogenic cancer." In any event, it is our opinion that the case for branchiogenic cancer is far from being conclusively established. As will be discussed in more detail later, the only absolute proof of the existence of a specific tumor such as branchiogenic cancer would be the histologic demonstration of cancer arising in the wall of a branchiogenic cyst; so far as is known, no well-documented case of this kind has ever been recorded.

REVIEW OF THE LITERATURE

Von Volkmann, in 1882, was the first to suggest that some cervical cancerous tumors might arise in the vestigia of branchial clefts.²⁴ He postulated such an origin after observing three patients with carcinomatous masses in the upper neck in whom he could discover no other primary lesion after direct visual and digital examination of the oral cavity and pharynx. At that time the laryngeal mirror, developed by Czermak in 1858, had not come into common

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use. Von Volkmann's discussion, based upon three short term case observations, was entirely theoretical; it is hardly correct, therefore, to credit him, as has been done, with having *shown* that certain cervical carcinomas are of branchiogenic origin.

In the progressive development of medical science there is a natural, though often erroneous, tendency to assume that a given disease originates at the site where symptoms first appear. Such a fallacious concept, as regards malignant tumors of the neck, is exemplified in John C. Warren's *Surgical Observations of Tumors* published in 1837. In this monograph²⁵ several operative cases are reported which are classified as "malignant scirrhus of the lymph glands of the neck" and "fungoides of the neck." Warren plainly implies that these tumors arose in the "glands" but in the light of present-day knowledge, their actual character can be suspected from the fact that in some of the cases he reported the growths eventually were found to extend to the "parietes of the pharynx." Such "extensions" of the tumor to the pharynx were undoubtedly the sites of the primary growths. Fifty-three years later (in 1935) Crile & Kearns⁵ arrived, by the same illogical reasoning, at the same dubious conclusions when they reported 28 cases of alleged branchiogenic cancer, none of which survived five years, and when they mentioned a case of their own which was first diagnosed as cancer of the larynx but "proved" at autopsy to be of branchiogenic origin, "invading the pyriform sinus."

Following Von Volkmann's original report the subject of branchiogenic cancer was not often mentioned in the medical literature but the tumor appears to have been generally accepted as being specific. In 1900 Nicholas Senn,²⁰ who wrote rather extensively on neoplastic diseases in general, apparently considered branchiogenic cancer of little significance, since he mentions no other growth except "chondroma branchiogenes" as arising in vestigial branchial clefts or branchial cysts. James Ewing,⁶ in 1919, although admitting that there was no specific histologic pattern characteristic of branchiogenic cancer, nevertheless appeared to accept Von Volkmann's theories. Curiously enough, however, Ewing, in his discussion of the subject, mentions difficulty in swallowing as one of the early symptoms, which suggests to us that in the cases he had discussed there were probably undetected pharyngeal primaries.

Almost from the beginning there have been some skeptics who questioned the existence of such an entity. In 1893, John Bland Sutton²¹ commented:

"One of the facts connected with epithelioma of the mucous membrane of the mouth—and it matters little whether the disease begins on the tongue, cheek, hard or soft palate, or gums—is the extraordinary size which the infected lymph glands in the neck sometimes attain, whilst the ulcer scarcely exceeds 1 cm. in diameter. This is worth bearing in mind, because an enlargement of the cervical lymph glands in individuals past middle age should always induce the surgeon to examine the various recesses of the mouth and fauces for small, inconspicuous epitheliomatous ulcers, and with every care they sometimes escape detection during life. It is necessary to emphasize this, because a good deal has been written about "branchiogenous cancer," or, as it is sometimes called, "malignant cyst" of the neck. The tumor is most commonly observed after the age of 50, and is

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deeply seated in the neck, usually near the fork of the carotid; it grows with great rapidity, and in many cases softens in the center and gives rise to fluctuation. The overlying skin becomes brawny and red, and the resemblance to an abscess is so striking that, in several cases, I have known a knife to be used under this impression. Gradually the implicated skin sloughs, and then an epitheliomatous chasm forms in the neck. Microscopically the tissue of these tumors is characteristic of epithelioma. Some writers are of opinion that these are primary epitheliomata, arising in remnants of branchial clefts. My belief is that, in most of the cases, these gland masses are secondary to epitheliomata originating in recesses of the pharynx or naso-pharynx, and the theory that they arise in remnants of branchial clefts is pure fiction."

Willis,²⁷ in 1934, is distinctly skeptical when he states that branchiogenic cancer should be "tolerated neither as a clinical diagnosis nor as a histologic finding on surgical material." Many authors in discussing branchiogenic cancer call attention to the possibility of silent primary lesions in the mouth and pharynx and emphasize the necessity for careful examination in these areas. A few mention the desirability of a five-year follow-up but, nevertheless, accept Von Volkmann's theory of branchiogenic origin of some cervical cancers and in their own cases appear willing to make such a diagnosis on minimal evidence.^{3, 4, 8, 13, 15-17, 19, 22}

In a survey of the medical literature on malignant branchioma we have found between 225 and 250 cases reported by 34 authors. The indefiniteness of this total is due to the vagueness and uncertainty of the authors in some of the reports. Of this total number of alleged cases it is not possible to accept more than three as presenting reasonable evidence of branchiogenic origin, as judged by the diagnostic criteria employed in the Head and Neck Clinic at the Memorial Hospital. These three cases (all five-year survivals after surgical excision of cervical carcinomas) are contained in a report of 80 alleged cases by Oliver.¹⁶ In the remaining 77 cases of Oliver's series the only evidence of branchioma was the failure to find a primary lesion during a short period of observation, before the patient was lost to follow-up or up to the time of death. No author except Oliver reports five-year survivals in alleged cases of branchioma, and it is certainly significant that in 96 per cent (77 cases) in Oliver's series there were no five-year survivals. In Oliver's report most of the cases are from the Laboratory of Surgical Pathology at the Johns Hopkins University and the patients were not personally observed. Many of them were reported as having died within two to three months after radical excision (neck dissection). The cause of death was not stated and even the question of recurrences was not discussed. It seems likely that many of these cases did die of undetected primary lesions elsewhere.

DEFINITION

The term, *branchiogenic cancer* refers to those malignant tumors which are believed to arise in vestigial remnants of branchial pouches (Lat. *branchia*; Gr. *Branchio* = gills). Most of the growths considered under this heading are epithelial in character, and therefore the designation *branchiogenic carcinoma* is frequently used as an all-inclusive term. Theoretically, connective tissue

growths could also arise in vestigial branchial remnants, so that the term *malignant branchioma* would be more specific.

In order to consider even the tentative diagnosis of branchiogenic cancer in a given case it is necessary to assume that the cervical tumor arose primarily in the neck. As will later be discussed in more detail, there are no histologic criteria which would serve to differentiate metastatic cancer from that arising in branchiogenic vestigia. Any clinical opinion that a given tumor originates primarily in the neck or in a branchial remnant must rest entirely upon the assumption that there is no other primary lesion elsewhere. Experience on the Head and Neck Service at the Memorial Hospital has shown that frequently cervical metastasis is the first, and for a long time the only symptom of silent or cryptic cancer in the upper respiratory and upper alimentary tracts. We have, therefore, established the following criteria to fulfill the requirements for even a tentative clinical diagnosis of branchiogenic cancer.

MEMORIAL HOSPITAL CRITERIA FOR THE TENTATIVE DIAGNOSIS OF BRANCHIOGENIC CANCER

1. The cervical tumor must have occurred somewhere along a line extending from a point just anterior to the tragus of the ear, downward along the anterior border of the sternomastoid muscle to the clavicle.
2. The histologic appearance of the growth must be consistent with an origin from tissue known to be present in branchial vestigia.
3. The patient must have survived and have been followed by periodic examinations for at least five years without the development of any other lesion which could possibly have been the primary tumor.
4. The best criterion of all would be the histologic demonstration of a cancer developing in the wall of an epithelial-lined cyst situated in the lateral aspect of the neck.

We have searched diligently over a period of several years to find a case in which cancer could be demonstrated to arise in the wall of an epithelial-lined cyst in the neck. A few years ago one of us studied 63 cases of branchiogenic cyst observed on the Head and Neck Service at the Memorial Hospital. The cysts had all been excised and examined histologically. In this group there were found three cases in which the question of malignant transformation arose at first, but more careful study of the tissue sections failed to disclose the necessary evidence in a single instance. Recently, there have come to our attention two other cases of cervical cysts in which the first histologic examination of the surgical specimen appeared to reveal both cancer and a benign cyst wall. After more careful study, however, it was the final opinion of the pathologist that such histologic evidence of cancer arising in a benign cyst wall was not present.

If cancer can arise in vestigial branchial remnants, then logically it could arise also in vestigia of thyroglossal ducts. Thyroglossal cysts are fairly common and are always found in the midline of the neck at about the level of the hyoid bone. Nevertheless, we have never observed cancer of epithelial origin arising at this site. In our opinion this observation in itself throws at least some

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doubt upon the validity of the theory of branchiogenic cancer. In this connection, it might be mentioned that cases of thyroid carcinoma arising from the thyroid tissue in thyroglossal cysts and tracts have been reported (but not epidermoid carcinoma).

The experience on the Head and Neck Service at the Memorial Hospital as regards the clinical course and morbid anatomy of head and neck cancer in general, has impelled the application of the rigid standards itemized above before even the tentative diagnosis of branchiogenic cancer can be considered. *We have followed too many cases in which cancer appeared first and apparently only in the neck, and in which a silent cryptic primary lesion elsewhere in the body became evident only after an extended interval up to four years, to permit us to accept the diagnosis of branchiogenic cancer under any other standards.* If these criteria are accepted, then there follows apparently the paradox that a patient cannot die of branchiogenic cancer within a five-year period. It is plain, however, that should such an entity exist, many patients would die of the disease within five years unless the growth were controlled.

Examples of typical cases in which a diagnosis of branchiogenic cancer might be made erroneously or on scant evidence are given below.

CASE REPORT

M. T., a physician, age 30, was seen first in September, 1945. He stated that 11 months previously (October, 1944) he had noted an enlarged "gland" in his left neck. At the time, he was interning in a large metropolitan hospital and for the succeeding period of 11 months consulted several members of the attending staff, receiving a variety of opinions; no biopsy was made, however, and no treatment was advised.

Physical Examination. At the first examination (September, 1945) a smooth, ovoid, moderately firm, non-tender, movable mass about 5 cm. in diameter was found lying under the anterior edge of the left sternomastoid muscle at about the level of the bifurcation of the carotid artery. Repeated examinations of the oral cavity, nasopharynx, hypopharynx and larynx and a general physical examination revealed no evidence of a primary lesion. Roentgenograms of the chest were negative. An aspiration biopsy of the cervical mass was made and the pathologic diagnosis was "metastatic epidermoid carcinoma." The pathologist suggested the nasopharynx as the most likely site of the primary lesion and the lung as the second most likely site.

After repeated examinations of the nasopharynx, a specimen was removed from a slightly raised area on the posterior nasopharyngeal wall which originally had been considered to be a normal anatomic variant. The histologic report of the biopsy was "normal pharyngeal tonsillar tissue." The findings in the nasopharynx were considered to be so indefinite that no further biopsy was attempted. In the face of negative findings for a primary lesion, treatment by radiation therapy was instituted to the cervical mass while the search for the primary lesion was continued. Over a period of 3 weeks the tumor received a total of 7000 r in divided doses with the following factors: 250 kv, 1½ mm. cu. filter, 50 cm. TSD, a single 6 cm. circular port; a total of 25 mc. of gold radon seeds were implanted through the skin into the tumor in 3 divided doses. The cervical mass regressed over a period of 6 weeks and has not recurred locally.

During the next 2 years a search for the primary lesion was continued and at each monthly follow-up visit the oral cavity, nasopharynx, and hypopharynx were examined thoroughly for a primary lesion. A total of 22 such negative examinations are recorded on the patient's clinical record. After a period of 2 years of apparent freedom from disease, the patient failed to keep his appointments and in response to inquiries replied by

letter that he had entered the practice of medicine and was too busy to take time out for further follow-up examination.

After an absence of about 1 year (4 years following the onset of symptoms and 3 years following treatment of the cervical mass) the patient re-appeared, stating that the main reason for failure to return for follow-up was that it depressed him to be examined regularly for what he knew had been cancer. About 6 weeks previously, in October, 1948, he had noted an enlargement of the lymph nodes in the right neck, impaired hearing in the right ear (4 weeks' duration) and some obstruction in the left side of the nose with recurrent nosebleeds (2 weeks' duration). Re-examination revealed the left nasal cavity to be blocked by a large necrotic mass, and on mirror examination a bulky tumor was found in the left nasopharynx, occluding the choana. A mass $2\frac{1}{2}$ cm. in diameter was found under the anterior edge of the sternomastoid muscle in the upper right neck. A biopsy of the nasopharyngeal tumor was made and a report returned of "epidermoid carcinoma."

The site of the original tumor in the left neck was free of palpable disease. Treatment was again instituted by radiation therapy and there was prompt regression of both the nasopharyngeal and cervical tumors. About one year later the patient developed generalized metastases.

Comment. This clinical report illustrates several important features to be kept in mind when considering a diagnosis of branchiogenic carcinoma. This case would have been accepted for a period of four years by many as one of branchiogenic cancer on the following basis: (1) a proved carcinomatous cervical tumor appearing in 1944 without evidence of any other primary lesion after 22 thorough examinations of the mouth and pharynx; (2) the patient remaining well without recurrence of cancer elsewhere for about four years following treatment of the cervical tumor. Then, as a final denouement, there appeared four years later a previously undetected growth in the nasopharynx. Only three of the reported cases of so-called branchiogenic carcinoma in the literature have presented such presumptive evidence for a period as long as four years.¹⁶ Nevertheless, the case reported above finally proved to be one of the common varieties of pharyngeal cancer in which cervical metastasis characteristically appears as the first symptom and in which the primary lesion remains silent (cervical metastasis appears as the first symptom in over 50 per cent of cases of cancer of the nasopharynx). It is particularly significant that the nasopharynx was suspected all along as the site of the primary lesion despite the fact that 22 examinations at monthly intervals for a period of two years failed to reveal it. This case report also illustrates the lack of justification for accepting the opinion of any examiner on a single or even multiple examinations as reliable proof of the absence of a primary lesion.*

* Typical but by no means unique examples of unwarranted case reports of branchiogenic carcinoma are the following:

Lillie, Cox, and Teufel¹⁰ report the case of a man, aged 55, with an "indurated ulcer of the lower lip" and a "hard, tender gland" in the left submaxillary region. Both lesions were excised and examined histologically. The ulcer of the lip was diagnosed as "epithelioma, grade I," and the submaxillary tumor as "malignant cyst, grade III." A few months later a second "malignant cyst" was removed from the right submaxillary region. Two and one half years later, a third "cyst" was removed from the submental region; the latter was also found to be a "malignant cyst." The authors disregard the fact that the clinical history was typical of cancer of the lip with cervical metastases. Attaching great

THE EMBRYONAL BRANCHIAL APPARATUS: DEVELOPMENTAL ANATOMY

The theory that lateral cervical cysts and fistulas may be related to some abnormality in the development of the branchial arches and pouches during embryologic life was first advanced by Acherson² in 1832. Since then, this basic hypothesis has received wide acceptance, although there have been some differences of opinion as to the precise details of the mechanism by which such abnormalities occur.

It is generally agreed by authorities in this specialized field of anatomy that there are four branchial pouches, separated by five branchial arches which develop through a combined interplay of ectoderm and entoderm. On the other hand, Wenglowski,²⁶ a Russian embryologist of considerable competence, believes that there are actually five and that the fifth groove in the arch gives rise to the thymus gland. From the entodermal primitive pharynx, four out-pouchings develop and advance toward four corresponding invaginations of the ectodermal precursor to the skin of the neck. This advance may progress until confluency of the two pouches occurs, but it usually stops short of this stage and regression sets in without continuity ever being established. The lining of all of these pouches consists of squamous epithelium. As the pharyngeal component advances, it may carry with it aggregates of lymphoid tissue (of the tonsillar type and lacking the peripheral sinuses of lymph nodes), mucous-secreting glands, and bits of smooth muscle. This series of events is usually first recognizable embryologically during the latter part of the first month of intra-uterine life and regression is well under way by the middle of the second month. In human beings, then, the process is of short duration and is usually complete within a month of its recognizable onset.

significance to the difference in grading of the tumors of the lip and neck, respectively, as reported by the pathologist, the authors conclude that the cervical tumors were "multiple branchiogenic carcinomas" arising in the second branchial and the "mesobranchial" (*sic*) clefts, respectively, in a patient with cancer of the lip.

A second example of an unwarranted diagnosis of branchiogenic carcinoma with an even more ingenious explanation is that of Vokoun.²³ He reports the case of a woman, age 44, who sought medical advice because of dysphagia of four months' duration. He states that a diagnosis of "tuberculosis of the larynx" had previously been made for the reason that "the larynx had a peculiar pallor of the roof—a condition many nose and throat men consider tuberculous." The author states that "under the right mandible, deep in the neck, was a tender, firm, fixed mass the size of an olive, directly beneath the angle of the jaw." A roentgenographic examination was made with the patient swallowing a barium mixture and "with considerable difficulty, she managed to force some of the mixture past the esophagus, which showed a constriction opposite the area of the tumor in the neck." After a preliminary gastrostomy, the cervical mass (the size of an olive) was surgically exposed and a specimen was removed for biopsy. The histologic examination revealed "sections of tumor tissue, embryonal in form, highly malignant in character."

Although the history and clinical setting were typical of cancer of the hypopharynx and upper end of the esophagus with cervical metastasis, and despite the fact that a cervical tumor "the size of an olive" could hardly by itself have caused dysphagia of four months' duration, nevertheless the author concludes that this was a "carcinoma arising from an epithelial rest in an obliterated (*sic*) branchial cleft."

Arey¹ considers the first branchial pouch as the precursor of the external auditory and auricular concha and the second pouch as the antecedent of the tonsillar fossa; the third and fourth grooves contribute to the development of the thymus and parathyroid glands. Wenglowksi agrees as far as the development of the first and second clefts are concerned; however, he distinguishes an anlage—which he calls the pharyngo-thymic duct—derived from the third and fourth pouches. This anlage is supposed to contribute to the development of the thymus and parathyroid glands and the lateral lobes of the thyroid gland. The fate of the fifth groove (ultimo-branchial body) remains controversial and attempts definitely to assign each individual case of branchiogenic cyst to an origin from a specific embryonic pouch are also likely to be challenged. In summary, an analysis of the accumulated evidence indicates that the second branchial groove is probably the origin of most branchial lesions that present in the neck.

In any case, branchiogenic cysts and branchiogenic cancer can theoretically arise anywhere between the level of the zygoma and the clavicle. The most common site of branchial cysts is at the level of the hyoid bone (third and fourth clefts).*

PATHOLOGY

Most experienced pathologists agree that there are no gross or microscopic features which could possibly differentiate cancer of metastatic and of branchiogenic origin, respectively. For this reason, a diagnosis of malignant branchioma is never even suggested by the Department of Pathology in Memorial Hospital.

In the present series, surgical specimens were available in five cases, and in these the tumors varied in size from 3.5 to 6 cm. in diameter. All were solitary tumors of smooth contour and firm consistency. In brief, no one specimen could be differentiated grossly from metastatic cervical cancer.

Histology. The diagnosis of cancer was proved in the 15 cases herein reported by means of aspiration biopsy in three cases, by incisional biopsy in

* It is curious that although the branchial apparatus in the embryo is situated along a line from the zygoma to the clavicle, nevertheless branchiogenic cysts are almost always found at the level of the carotid bifurcation. Any cyst in the lateral aspect of the neck above or below this level should be viewed with suspicion as regards its branchiogenic origin. In two cases recently observed by us there were cysts just above the middle of the clavicle, both proved by aspiration to contain clear straw-colored fluid. Both were diagnosed clinically as of branchiogenic origin and at operation from the standpoint of surgical anatomy were thought to be branchiogenic cysts. Nevertheless, histologic examination of the excised specimens showed small areas of papillary adenocarcinoma, thyroid type. With this discovery the diagnosis was changed to thyroid cancer (cryptic primary) with cervical metastasis. Hemithyroidectomy and neck dissection were performed on the homolateral sides and the surgical specimens in both cases showed primary carcinoma in the corresponding thyroid lobe, with metastases to several lymph nodes. These experiences raise some doubt in our minds as to the validity of a diagnosis of branchiogenic cyst for lesions situated in the lateral aspects of the neck either above or below the level of the hyoid bone. It must be admitted, however, that these observations by themselves could not be used as evidence against branchiogenic cancer, since in most of the alleged cases the tumor is also reported to be located near the level of the hyoid bone.

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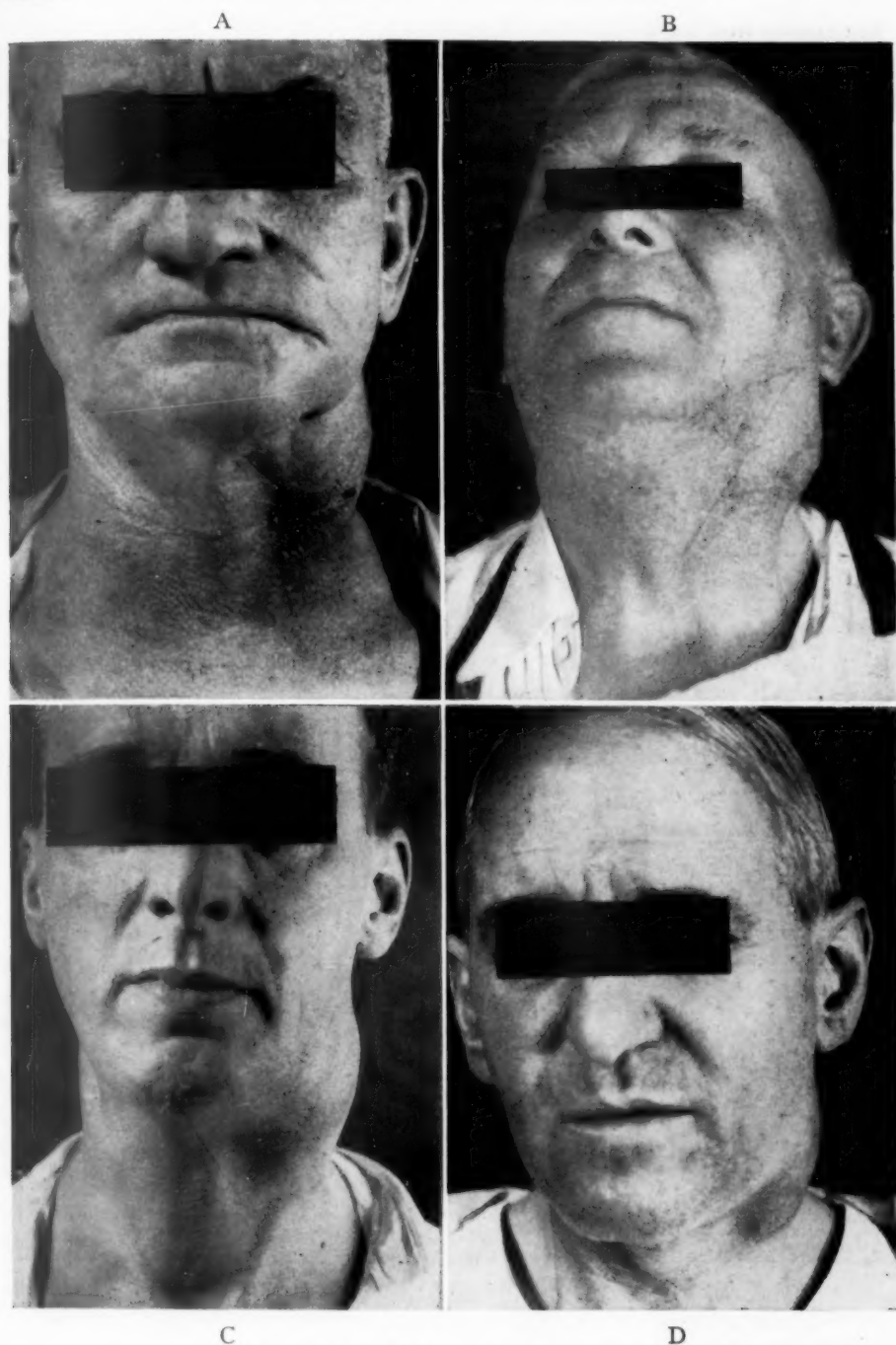


FIG. 1.—*So-Called Branchiogenic Cancer Possesses No Clinical Characteristics Permitting Differentiation From Other Forms of Cervical Tumors.* Despite the fact that all of the above four patients present an identical picture on clinical examination, a different etiology for the cervical mass exists for each case: (a) primary undetermined (b) floor of mouth primary (c) nasopharynx primary (d) tongue primary.

five and by histologic study of the surgical specimens in six. In nine instances the diagnosis was established from submitted microscopic slides (incisional biopsy made before the patient came to the Memorial Hospital). In the present series the histologic diagnoses were: epidermoid carcinoma (seven cases), squamous carcinoma (six cases), adenocarcinoma (one case), and anaplastic carcinoma (one case). Oliver¹⁶ and others infer that there are characteristic histologic patterns in branchiogenic cancer. In none of our cases was the

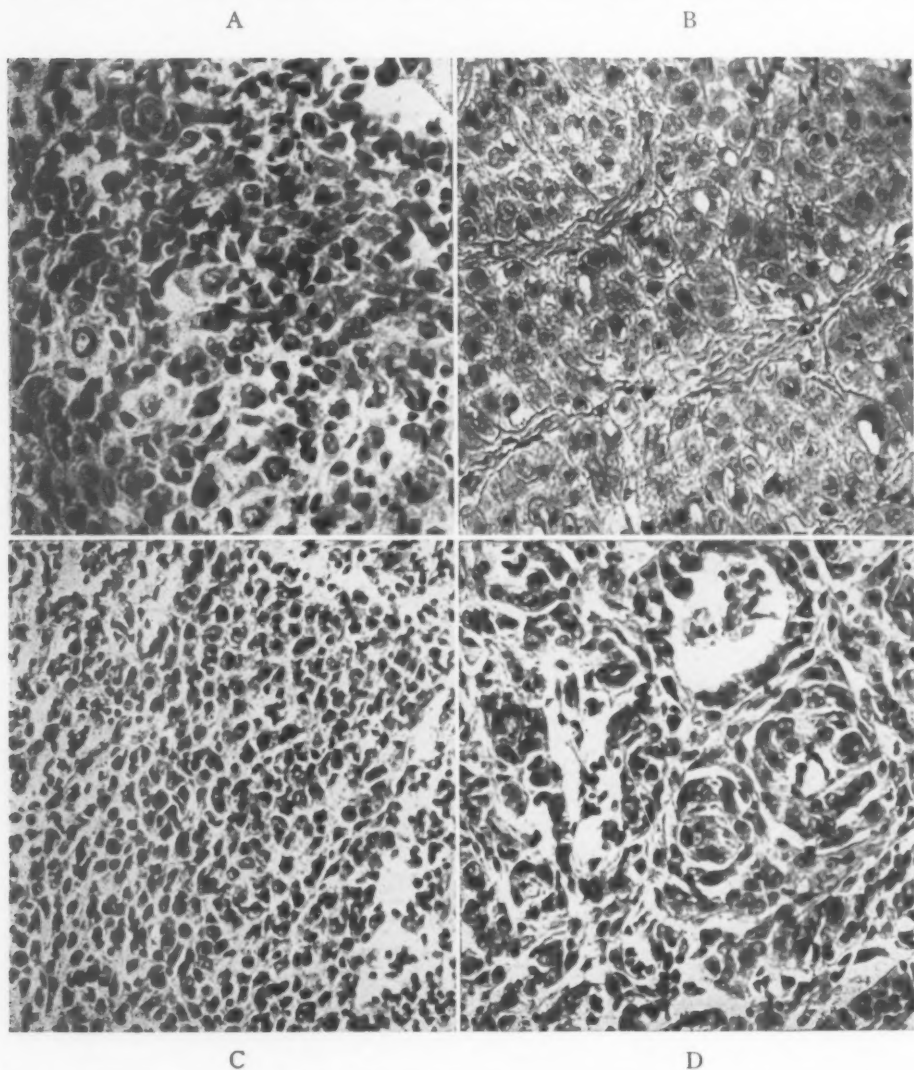


FIG. 2.—So-Called Branchiogenic Cancer Possesses No Microscopic Characteristics Permitting Differentiation From Cervical Metastasis Secondary to Primary Tumors Occurring in the Mouth and Pharynx. A, B, C, and D are representative microphotographs from neck masses present in the patients shown in Figure 1. The pathologists report was squamous or epidermoid carcinoma in all four specimens and it can be seen that so-called branchiogenic carcinoma possesses no characteristics, clinical or histologic, permitting recognition as a specific entity.

THE CASE FOR BRANCHIOGENIC CANCER

histologic appearance different from the ordinary run of cervical metastatic carcinoma secondary to primary lesions in the upper respiratory or upper gastro-intestinal tracts (Figs. 1 and 2).

ETIOLOGY, SYMPTOMATOLOGY AND CLINICAL COURSE IN 15 CASES OF CERVICAL CARCINOMA WITHOUT ANY OTHER DEMONSTRABLE PRIMARY TUMOR SURVIVING FIVE YEARS FOLLOWING TREATMENT

An analysis of the cases herein presented reveals no clinical features differing from metastatic cervical cancer except for the fact that no other primary lesion was found in any of the cases. There was only one prominent symptom, namely, the presence of a cervical tumor which proved to be epidermoid carcinoma or adenocarcinoma on histologic examination. The clinical course up to the time of admission was slow and uncomplicated in all instances.

Incidence. The observation of a patient for five years following treatment of a solitary carcinomatous mass in the neck without the discovery of any other primary lesion is rarely encountered at the Memorial Hospital. During the eight-year period, 1933-1940, inclusive, over 5000 new cases of primary malignant tumors above the level of the clavicle were observed on the Head and Neck Service and only 15 cases (0.3 per cent) were encountered which might be tentatively classified as branchiogenic cancer. For purposes of comparison it may be significant to mention that during the eight-year period when these cases were observed, there were 450 cases of cancer of the lip, 470 cases of cancer of the tongue, and about 470 cases of cancer of the larynx.

Age and Sex. In the 15 cases considered in this report, 12 of the patients (80 per cent) were more than 50 years old; in about half of the patients the tumor appeared after the age of 60. This age incidence is identical with that of cancer of the mouth and pharynx. The youngest patient was ten and the oldest 72 years of age. Parkinson¹⁷ has reported an alleged case of branchiogenic cancer in a seven-year-old male followed for 2½ years after surgical removal of a cervical tumor which proved to be epidermoid carcinoma. The follow-up period is too short for the acceptance of this tumor as one of branchiogenic origin.

In the present series there were 13 males and two females; this sex incidence approximates that of mouth and pharyngeal cancer in general. McWhorter¹³ reports a ratio of three males to one female, and Oliver¹⁶ a ratio of nine to one, in their respective series. Hertzler⁷ makes the surprising statement that branchiogenic carcinomas "occur most frequently in aged females."

Duration of Symptoms. In this series the average duration of symptoms, that is, the presence of a "lump in the neck," was two months, and the range from one week to two years. Cases such as one of those reported by Oliver,¹⁶ where a mass had been present since birth in a 54-year-old woman, and those reported by others in which a tumor had been present for 16, 19, and 34 years, respectively, have never been observed at the Memorial Hospital. If such cases were of true branchiogenic origin, the growth could have developed in pre-existing branchiogenic cysts.

Location of the Tumor. As previously stated, branchiogenic cysts can occur anywhere along a line beginning just in front of the tragus of the ear and running downward along the anterior border of the sternomastoid muscle to the clavicle. It is significant, however, that in all of our cases the tumors appeared at about the level of the hyoid bone, the site of the highest nodes in the internal jugular chain and in which cervical metastases are most likely to appear from a primary lesion in the oral cavity or pharynx. There was an equal predilection for the right and left sides of the neck.

Size. In the present series the range in the size of the cervical tumors when the patient first reported to the Memorial Hospital was between 3.5 to 8 cm. in diameter, with a median size of about 5.5 cm.

Pain. None of our patients complained of pain and in our opinion there is no factual basis for such assertions as that of Crile⁵ who says of branchiogenic carcinoma, "the occurrence of pain is fairly frequent." Hertzler's⁷ statement that in malignant branchioma pain is often referred to the ear seems to us to be of little significance, since bulky infiltrating metastatic masses in the upper neck frequently produce pain in the ear (reflex through the vagus and/or cervical nerves).

Clinical Characteristics. In our cases there were no anatomic or clinical characteristics differing from those found in metastatic cervical cancer. In brief, the cervical tumors were ovoid, firm, non-tender, movable masses, all located somewhere along the course of the internal jugular vein, in the same location where metastatic cervical cancer is most frequently found.

Methods of Treatment Employed. The clinicians on the Head and Neck Service at the Memorial Hospital have always been surgeons who have themselves employed surgery or radiation therapy, or a combination of the two, as indicated in the individual case. Although the members of the staff have always been reluctant to operate on patients with cervical carcinomatous tumors without demonstrable primary lesions, nevertheless, over the period of the last 25 years there were many cases in which the patients have been operated upon as well as irradiated. It is significant that in 14 out of 15 patients with cervical carcinomatous tumors but without a demonstrable primary lesion who have survived five years or more, the treatment has been by radiation therapy. In only one case (a 12-year-old girl with adenocarcinoma) was surgery alone employed. The fact that in our series there is only one five-year survival following surgery and 14 following radiation therapy suggests not only the possibility but even the probability that in many, if not all, of these irradiated cases there was a primary lesion in the pharynx which fell within the beam of cancer-lethal radiation and that in these cases such a primary lesion was controlled without ever being discovered.* From the standpoint of the morbid

* Several cases have been observed at Memorial Hospital with residual cancer in the neck following radiation therapy given elsewhere, in which on the basis of histologic examination of the cervical tumor and symptoms associated with the beginning of the illness the former presence of a primary lesion in the nasopharynx seemed likely; in these cases, however, a physical examination at the time of admission to Memorial Hos-

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anatomy of a primary lesion in the pharynx and metastasis in the neck, the two might readily lie within 1 to 3 cm. of each other, and from the physical standpoint the distribution of the tissue dose of radiation would be such as to make it entirely possible for the undiscovered small primary to be sterilized at the same time as the cervical mass.

The methods of radiation therapy employed were fractionated roentgen radiation alone in two cases, the dosage varying from $3600\text{ r} \times 2$ to $4000\text{ r} \times 2$ (200—250 kv, 1.5 mm. copper filter; 50 cm. TSD 3.5—7 cm. circular ports); in five cases of fractionated irradiation, in dosages about as previously mentioned, there was supplementary implantation of gold radon seeds in doses of 20-30 mcs; in six cases interstitial radiation alone, in doses varying from 30-56 mcs., was used; in five cases surgery was employed (local excision or radical neck dissection) either preceding or following radiation therapy. From this résumé of the treatment factors it can be seen that the radiation dosage was in the cancer-lethal range, and that it was often found to be successful in mouth or pharyngeal cancer.

In a single case of the present series, surgical excision alone was employed for a solitary tumor situated in the upper neck in a girl ten years of age. Neither by the findings at operation nor by the histologic examination of the surgical specimen can it be definitely stated that the tumor might not have arisen in the tail of the parotid salivary gland. The case is included here as a concrete example of the negative character of all recorded evidence for the branchiogenic origin of any cervical tumor; in brief, although we have recorded in this report 18 cases (including Oliver's three cases), nevertheless we must conclude that the evidence for such an origin of cervical cancer remains unproved.

DIAGNOSIS

The relative importance of the subject of branchiogenic cancer should not be judged solely on the basis of its doubtful identity or at least its rare incidence, for in doing so one would be inclined to relegate this hypothetical tumor to a status no more significant than that of a medical curiosity. The importance of the subject lies rather in the frequency with which the diagnosis of branchioma is unjustifiably made in cases where the patient complains only of a cervical mass and in which no other focus of growth is discovered immediately or even by repeated examinations. When a final diagnosis of malignant branchioma is made on such tenuous and scant evidence, it naturally follows that treatment will be given only to the cervical mass and that no further search for a primary lesion will be made. Since it is axiomatic that the cure of cancer is not possible without aggressive treatment directed to the primary growth

pital failed to reveal any such growth. In some, the therapist had given radiation directed to the center of the head (through the face, top of the head, occiput and the sides) for the sole reason that some consultant had suggested the possibility of that vague entity sometimes referred to as a "Schminke tumor" (a loosely-used term referring to anaplastic carcinoma located somewhere in the pharynx), but had never established the presence of such a lesion by clinical examination, biopsy, and histologic confirmation.

itself as well as to the metastasis, all patients in whom an erroneous diagnosis of branchiogenic cancer is made and persisted in are doomed to die of cancer, unless by accident the primary lesion should happen to lie within the beam of radiation. *In these facts lie the main importance of the subject of malignant branchioma.* Von Volkmann's²⁴ belief that the cervical tumors in his three cases arose primarily in branchiogenic remnants was based solely on the fact that he did not discover a primary lesion in the mouth or pharynx by inspecting the mouth and exploring the pharynx with a palpating finger. After almost 70 years, the uncritical and haphazard acceptance of the diagnosis continues and cases of alleged branchiogenic cancer are still reported, even though they are poorly documented and supported by only flimsy evidence.

The naïve confidence that a single and often casual examination of the oral cavity and pharynx permanently and unequivocally rules out the possibility of a primary lesion in these regions is widely held at the present time despite the fact that about 60 years ago at least one observer knew enough about the clinical behavior of oral and pharyngeal cancer to utter plain words of caution in this regard. Sutton²¹ merely called attention to the possibility of an obvious primary which could be discovered if a competent search were made. With our present-day knowledge, however, we know that not only may a silent primary often be discovered by a thorough examination when the patient first comes for treatment, but that a cryptic primary in the mouth or pharynx may first become apparent after repeated examinations as long as four years after the initial appearance of a cervical metastasis.

Reports in the literature regarding the greater frequency of branchiogenic cancer are unacceptable after critical review. For instance, Pizetti¹⁸ reviews a series of 100 cases of lateral cervical carcinomatous tumors in which he designates 11 as branchioma; in none of these are the rigid criteria previously listed in the present study met. In one of Pizetti's patients the growth "invades the pharynx," and it is rather obvious that in this case he was dealing with pharyngeal cancer metastatic to the cervical lymph nodes. In general, this series of supposed branchiogenic cancers are so poorly documented that such a diagnosis could hardly be considered even from a speculative standpoint. In the current medical literature^{5, 8, 19} branchiogenic cancer is often discussed with unwarranted confidence, supplemented with published photographs of patients but without any suggestion that the diagnosis of the tumor is difficult and uncertain. Such a bland attitude serves only to perpetuate the confusion as regards this theoretical entity. In our opinion the subject of branchiogenic cancer should not be discussed in the literature unless the reader is cautioned as to the rarity of the tumor (if it does exist) and the uncertainty and complexities of the diagnosis.

In a recent publication¹⁴ we have called attention to the frequency with which cervical metastasis occurs as the first symptom of cancer of the mouth and pharynx. Cervical metastasis with a silent primary lesion occurs in about 8 per cent of all cases of cancer of the mouth, pharynx and thyroid gland. Differently stated, in a consecutive series of about 3900 cases of cancer of the

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head and neck, cervical metastasis was the first symptom in 218 (about 5 per cent) while in specific areas, such as the mouth, pharynx, or thyroid gland, cervical metastasis with no complaint referable to a primary lesion is present in 8 per cent. In cancer of the nasopharynx, cervical metastasis is the first and for a time the only symptom in about one-third of the cases, and in only 70 per cent is the primary lesion discovered within a period of six months.

The basic truths clearly stated by Sutton more than one-half a century ago are largely disregarded by many observers, who appear willing to make definite diagnoses of branchiogenic cancer after a single negative examination for a primary lesion, or in other cases make such a diagnosis without waiting for the longer period, during which time a cryptic primary may be discovered. While most authors agree with these precepts in theory, they almost invariably disregard them in practice and in reporting their own cases. Others apparently place undue emphasis on postmortem findings when the necropsy examination reveals no evidence of a primary lesion. The clinician who has repeatedly searched for and finally found small silent primaries in the nasopharynx, tonsil or base of the tongue, will have little confidence in the ability of the pathologist to explore sufficiently all of these relatively remote areas to rule out with assurance the presence of a primary lesion by postmortem examination.

It is fallacious and even misleading to suggest that there are significant differences in contour, consistency, mobility and tenderness in the differential diagnosis of such lesions as branchiogenic cancer, metastatic cancer, melanoma, Hodgkin's disease, lymphosarcoma, etc. It was formerly considered a mark of clinical erudition and diagnostic acumen to memorize lists of differential criteria to distinguish clinically such diseases as tuberculosis, syphilis, and the sub-varieties of cancer, but in recent years with the development of dependable laboratory tests much of this purely inductive method of diagnosis has proved to be unreliable and impractical.*

In brief, the diagnosis of branchiogenic cancer is too frequently and too loosely made, and it is fair to state that the over-all competence as regards the knowledge of cancer can be fairly well judged, either in the individual surgeon or in a tumor clinic, as being inversely proportional to the frequency and confidence with which the diagnosis of branchiogenic cancer is made.

After several months were spent in collecting and analyzing the evidence and in preparing the preliminary drafts of this paper, we began to have serious doubts as to whether there was any dependable evidence either in the literature or in our own material to prove the existence of such an entity as branchiogenic cancer.

* One of us (H. M.) can remember back 25 years when a distinguished surgeon of that day confidently stated that he could differentiate such diseases as melanoma, Hodgkin's disease and metastatic cancer by palpation alone. He steadfastly maintained this view-point, although he was repeatedly proved wrong by subsequent biopsy. We have observed many cases in which there was a maximum range of variation in the consistency of tumor masses, supposedly characteristic of growths such as lymphosarcoma, melanoma, Hodgkin's disease and metastatic cancer.

THE CASE FOR AND AGAINST BRANCHIOGENIC CANCER

Up to this point in the present report it has been repeatedly implied that we have considerable doubt as to the actual existence of such a clinical and pathologic entity as branchiogenic cancer, but we have also stated that we know of no better explanation for the histogenesis of certain cervical cancerous tumors. Throughout the present discussion attention has been called to the frequency with which a diagnosis of branchiogenic carcinoma is made on inadequate evidence. Accordingly, the evidence both for and against the existence of a tumor of such origin will be examined, and the various possibilities considered.

When a patient with a cervical carcinomatous tumor and no other demonstrable primary lesion survives for a period of five years following treatment to the cervical mass only, can one state that the cervical tumor was the only focus of the growth, and in addition, that it was of branchiogenic origin? Such a conclusion must necessarily be based upon circumstantial evidence, for as previously mentioned, there are no histologic criteria to prove the branchiogenic origin of a cervical malignant epithelial tumor. So far no case has been reported in which cancer has been found arising in a branchial cyst or in any recognizable remnant of the embryonal branchial apparatus. If a carcinomatous tumor of the neck does not arise in a vestigial remnant, is there any other reasonable explanation for the histogenesis of the cervical cancer? Several of these possibilities will now be discussed.

Evaluation of the Evidence for Branchiogenic Origin in 15 Reported Cases of Cervical Cancer. The 15 cases herein reported fulfill the criteria for malignant branchioma previously referred to, that is, cervical carcinomatous tumors occurring in the lateral aspects of the neck, histologically proved, without any other demonstrable primary lesion, treatment given to the cervical tumor alone, and the patient followed systematically without recurrence for a period of at least five years. As we have previously mentioned, only three reported cases in the literature so far have fulfilled these criteria. Nevertheless, radiation therapy was used in 14 of our 15 cases and although four of these had surgery, the surgery itself cannot be given complete credit for the cure. In all cases the radiation dosage was within the cancer-lethal range. It is entirely possible that a primary undetected lesion existed, that it was situated within the beam of cancer-lethal radiation and that it never became clinically evident (base of tongue, tonsil, pharyngeal wall, extrinsic larynx).

Metastatic Carcinoma with Spontaneous Regression of the Primary Lesion. A number of cases are on record (6, 11, 12) in which histologically proved cancer, both primary and metastatic, have been observed to disappear without any treatment whatever. In any alleged case of branchiogenic cancer, therefore, it is theoretically possible that the primary lesion in the mouth or pharynx did regress spontaneously while the metastasis persisted. Although this explanation will probably not be acceptable, to many, nevertheless, it has actually more factual evidence to support it than does the theory of branchiogenic

origin, for while spontaneous regression of malignant tumors has been observed, the origin of cancer in the wall of a branchiogenic cyst has not.

In the Head and Neck Clinic at the Memorial Hospital several cases, not included in this report, have been encountered in which there were numerous cervical tumors, apparently multiple metastatic nodes, in which, following treatment by radiation and/or surgery, the patients remained well for more than five years without the discovery of any primary lesion. In these cases the simultaneous appearance of multiple enlarged nodes, occasionally bilateral, was such as to make the diagnosis of cancer of branchiogenic origin extremely remote, so that we have not even included them in the 15 cases considered in this report. In clinics where large numbers of cancer patients are observed, cases will occasionally be seen in which the clinical behaviour is so bizarre and unusual that it is impossible to classify them either clinically or anatomically. In many of these the evidence strongly suggests that the primary lesion may have regressed spontaneously.

Cancer in Epithelial Rests in Lymph Nodes. One of the theories in support of the primary origin of certain cancers in the neck is that they arise from epithelial rests in lymph nodes. Some years ago James Ewing, in a personal communication, stated to one of us that he had observed remnants of glandular acini in cervical lymph nodes which he interpreted as embryonal rests, but conceded at that time that he had never seen any remnants of squamous epithelium in lymph nodes which could possibly be of branchial cleft origin. In a personal communication, Fred Stewart stated that he has never observed any structural components in normal cervical lymph nodes which he could interpret as being of epithelial origin. In brief, the theory that cervical carcinoma can arise in epithelial rests in lymph nodes is even less tenable than that they arise in branchial remnants.

The Significance of the Absence of Even a Single Case Report with Cancer in the Wall of a Branchiogenic Cyst. Branchiogenic cysts occur with relative frequency and constitute one of the most readily identifiable varieties of cysts which originate from the embryonal branchial apparatus. If cancer can arise in vestigial branchial remnants, it would seem almost inevitable that in an appreciable number of cases observed over a long period of years cancer would be found in the wall of a branchiogenic cyst or lateral cervical fistula. So far as we know, no such case has ever been reported; in a series of 63 cases of branchiogenic cysts studied by one of us, there were one or two in which the question of malignant transformation was first considered but subsequent examination revealed no evidence that such a diagnosis was warranted. In our opinion, acceptable proof that such a tumor as branchiogenic cancer does exist must await the demonstration of cancer arising in such a cyst. The demonstration of such a phenomenon would represent the evidence *prima facie* in the case for branchiogenic cancer. All efforts to prove such a case have already been discussed in this paper.

THE CLINICAL MANAGEMENT IN CASES OF CERVICAL CARCINOMA
WITHOUT ANY OTHER DEMONSTRABLE PRIMARY LESION

Since in any given case of cervical tumor a diagnosis of branchiogenic cancer must remain uncertain and highly improbable for many months or even years, it is hardly logical to propose a specific plan of treatment for this particular growth. It seems rather more reasonable to discuss the immediate management of *those malignant cervical tumors which might be branchioma but which nevertheless are probably not on the basis of chance alone.*

Consider then the case of the patient who presents only a cervical mass and in whom there can be demonstrated at first no other focus of growth as a possible primary lesion. What sequence of procedures should be followed in such a case to establish a diagnosis and give the patient the greatest possible chance of permanent cure? Among the alternatives are (1) aspiration biopsy (2) incisional biopsy (3) radiation therapy (4) local excision of the mass and (5) unilateral neck dissection. Whatever is done, *the search for a primary lesion should never be relaxed.*

Aspiration Biopsy. One of the clearest indications for aspiration biopsy is a cervical tumor of an undetermined nature, since the procedure is both rapid and safe and, in addition, does not alter the clinical setting. Should the sectioned plug of tissue show epidermoid carcinoma, the probabilities are that there is a cryptic primary lesion somewhere in the oral or pharyngeal mucous membranes. Search should be continued indefinitely for such a primary lesion. Should the sectioned plug of tissue reveal adenocarcinoma, particular attention should then be given to the thyroid and major salivary glands, lung, pancreas, gastro-intestinal and urologic tracts as possible sources of the primary growth. If the aspirated specimen shows lymphoid tissue only, further help should be sought from the pathologist to determine the possibility of lymphomatous disease or whether the cells are non-neoplastic, in which case a further aspiration biopsy may be indicated. Only if the report is "epidermoid carcinoma" need any serious thought be given even to the remote possibility of branchiogenic carcinoma and if repeated examinations over a period of several days fail to disclose any primary lesion, consideration must then be given to the management of the known cancerous cervical mass.

Incisional Biopsy. The partial surgical removal of a mass for diagnostic purposes* is always objectionable and should be avoided if there is any alternative procedure. Incisional biopsy will seldom be indicated if aspiration biopsy is performed competently. When repeated aspiration biopsy has failed to provide a positive histologic diagnosis, due consideration should be given to complete (rather than partial) excision of the mass. In our series, incisional biopsy had been carried out before referral to us in six (almost half) of the cases. The resultant scarring and local extension of the growth in the operative

* *Incisional biopsy* may be defined as cutting into a tumor mass and removing a fragment for biopsy, while *excisional biopsy* may be referred to as the removal of all of the local tumor or enlarged lymph node. The first procedure is objectionable and should be avoided if the entire mass can be excised.

area from such a procedure is a serious handicap to subsequent successful treatment by any method.

Local Excision. If a cervical tumor has been proved to be carcinoma by aspiration biopsy (or other means), a simple local excision without any supplementary treatment is, in our opinion, inadequate. In most cases wider surgical excision, that is, block neck dissection is clearly indicated. In the present series simple local excision had been carried out elsewhere in four cases and the patients were subsequently referred to Memorial Hospital because of local recurrences.

In any case, to perform a local excision of a cervical mass immediately on admission seems to us a rather haphazard and irresponsible procedure. Such local excisions are frequently carried out by surgeons as the initial diagnostic procedure and after the pathologist's report of a malignant tumor has been made the patient is either discharged with no provision for follow-up or sometimes urgently referred to a tumor clinic, the surgeon being obviously relieved to wash his hands of the whole affair. Such a routine is to be unequivocally condemned. The surgeon should either withhold any operative procedure or should assume complete and permanent responsibility for his initial surgery.

Radiation Therapy. The conscientious surgeon experienced in the clinical management of cancer will be somewhat loathe to propose immediate surgery in proved cases of cancerous cervical tumors. He will dread the possibility that within a few days, weeks or months after excision of the mass, a primary lesion in the mouth or pharynx (or elsewhere) will become evident. Furthermore, he will realize that his surgery has not only been useless, but even meddling, in that the protective screen of lymphatics which stands between the primary lesion and the systemic lymph channels has been removed.

For these reasons, after a positive report of cancer from aspiration biopsy has been obtained, it is more prudent to defer surgery and apply radiation therapy to the cervical mass while continuing the search for a primary lesion. In most cases a combination of fractionated roentgen radiation and gold radon seeds will permanently sterilize the local tumor while preserving intact what remains of the protective screen of lymphatics. Under such a plan, should a primary lesion appear later (which it usually does), treatment can be instituted to the primary growth and to any metastasis with the assurance that previous radiation therapy has not seriously affected the clinical setting.

Neck Dissection. When the cervical tumor is larger than 3 to 4 cm. in diameter, consideration should be given to the serious sequelae incident to the necessary large cancer-lethal dose of radiation. In these bulky tumors radical neck dissection of the affected side may often be preferable to radiation therapy. The term "radical neck dissection," as used in our clinic means the removal of the sternomastoid muscle, internal jugular vein, submaxillary salivary gland and all lymphatics of the affected side of the neck from the inferior border of the mandible above to the clavicle below and from the midline of the neck to the anterior edge of the trapezius posteriorly.

Neck dissection is referred to at this point mainly as an alternative to

radiation therapy in large cancerous cervical tumors, although it was not employed in any of the 15 cases included in this report. Frequently, when we resort to neck dissection in cases of bulky cervical cancers of doubtful origin, a small primary growth in the thyroid gland previously obscured by the large metastasis is found in the surgical specimen by the pathologist. With thorough and planned clinical investigation of cervical tumors, radical neck dissection will seldom be indicated except for proved metastatic cancer and a definitely established primary lesion.

In brief, then, we advise a cautious approach to the problem of the management of cancerous cervical tumors without any other obvious primary lesion. If the mass appears clinically and histologically to be amenable to radiation therapy, we recommend that procedure while the search for a primary tumor continues. Should the cervical tumor appear to be too bulky or radioresistant, it is best to perform radical neck dissection of the affected side rather than mere local excision. Incisional biopsy is to be condemned as the initial diagnostic procedure.

SUMMATION AND EVALUATION OF THE EVIDENCE

When a theory has been passively accepted for more than 70 years and become ingrained in medical thought, it is obviously difficult to uproot it on presumptive evidence alone, despite the fact that the original theory itself was based on presumptive evidence. The hypothesis that cancer can and does arise in branchial remnants is attractive and admittedly a ready explanation for the histogenesis of certain cervical tumors. What then should be the current attitude toward this problem?

When the analysis of the clinical data preparatory to making this report was begun, we assumed that the existence of branchiogenic cancer was proved and proposed mainly to call attention to the fact that the diagnosis should be made guardedly, and to point out that in most cases the diagnosis was too loosely and too confidently made. In attempting to reduce the mass of presumptive evidence to concrete, indisputable facts we finally were forced to the conclusion that there is at the present writing no proof available to support belief in the existence of such a tumor. On the other hand, there is no better explanation as to the nature of certain cervical tumors, and it therefore must be admitted that the problem is unproved either for or against the existence of branchiogenic cancer.

SUMMARY AND CONCLUSIONS

1. The actual existence of a clinical entity deserving the specific term *branchiogenic cancer*, is entirely hypothetical.
2. There may be no other more reasonable explanation for the origin of certain rare cervical tumors.
3. A definite diagnosis of branchiogenic cancer cannot be made on a histologic basis.
4. The diagnosis of branchiogenic cancer in a given case of cervical tumor should always remain tentative and should never even be considered unless the

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patient has survived for a period of at least five years without the discovery of any other primary lesion.

5. A systematic plan for the management of these selected cases of cervical carcinomatous tumors is presented.

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THE DIFFERENTIAL DIAGNOSIS OF MALIGNANT BONE TUMORS*

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CERTAIN ADVANCES HAVE BEEN MADE in the over-all knowledge of bone tumors in the past ten years. Although these advances in knowledge of the subject seem to be made slowly, they are important, and there is every reason to be optimistic about the future; further strides are bound to occur. Some of the more important recent contributions which are helpful in making a diagnosis of bone tumor are: (1) the development and interpretation of the sedimentation rate of erythrocytes, (2) the utilization of the bone marrow biopsy, (3) the entire subject of tumor cytology and its value when used in conjunction with needle biopsy, (4) the application of Broders' grading of degree of malignancy to bone tumors, and (5) further microscopic differentiation of tumors, such as osteoid osteoma, eosinophilic granuloma and reticulum-cell sarcoma.

As with other types of malignant lesions, successful treatment of bone sarcoma depends on early and accurate diagnosis. The earlier the diagnosis the less danger of loss of a functioning part, or of life itself. An accurate diagnosis is almost as important as an early diagnosis, for it indicates the treatment to be employed. The types of bone tumors must be distinguished from each other; it must be determined if they are benign or malignant; and traumatic and inflammatory lesions which simulate bone tumors must be differentiated.

INCIDENCE

Malignant tumors of bone are relatively rare in occurrence when compared with other types of malignant lesions; yet Phemister¹ has stated that sarcoma of bone is the most frequent of all the sarcomas. Bone sarcoma has one main difference from other malignant lesions in that it most often affects relatively young persons. Its highest point of incidence is among persons of 15 to 20 years of age, according to statistics compiled by Christensen.² Plans for cancer detection, therefore, must include this age group, if persons suffering from malignant tumors of bone are to benefit under any mass tumor detection program.

Mayo Clinic statistics, recently compiled by Meyerding and Jackson,³ show that in 75 per cent of cases osteogenic sarcoma occurs about the knee. This localization to the lower end of the femur and the upper end of the tibia and fibula in three fourths of all cases of osteogenic sarcoma is extremely significant. It proves, in my opinion, that trauma, occurring as it does so frequently

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about the knee, is a definite inciting factor in the production of certain malignant bone tumors.

SYMPTOMS

Pain, intermittent or continuous, is the symptom of importance in bone tumors, and usually far precedes any objective evidence of a tumor. Pain in the region of a bone must always be carefully investigated, and not diagnosed as rheumatism, "growing pains" or a sprain, until the possibility of a bone tumor has been ruled out by a roentgenogram at least. Occasionally in lower extremities a limp will precede the actual occurrence of pain, and of course in later cases, swelling is evident to the patient and to the examining physician.

DIAGNOSIS

Once a bone lesion is discovered, it would seem that only biopsy of the lesion is needed in order to furnish data to make the diagnosis. Such a simple solution is not, unfortunately, always the case. It is true that the microscopic examination of the tissue is the one most valuable aid, but the diagnosis of a given bone tumor rests on more than this alone. One hundred per cent accuracy in diagnosis from tissue section is not possible for several reasons: (1) the tumor may have been previously irradiated, and this irradiation may have caused some change in the structure and appearance of the cells; (2) previous removal of a specimen for biopsy may have resulted in infection or hemorrhage or both, which may confuse the microscopic picture; (3) the surgeon may not take a representative section of the tumor, or may miss the main substance entirely; and (4) the pathologist may incorrectly interpret the tissue given him. It follows, therefore, that we physicians must use every means at our disposal to arrive at the proper diagnosis. This implies a careful history, with emphasis on the date and first occurrence of pain, the presence of swelling, history of injury, presence of chills or fever, and involvement of other parts of the body. A complete physical examination should then be done. Laboratory studies should include, as a minimum, urinalysis, determination of the concentration of hemoglobin, leukocyte count, flocculation test for syphilis and sedimentation rate. Further tests, such as those for serum phosphatase, differential blood cell count, biopsy of bone marrow, and study of special blood smears for morphologic changes may be indicated. Roentgenographic examination of the affected part and of the thorax should always be made. Not until all the information thus gathered is carefully assayed is biopsy justifiable, as case 1 will illustrate.

Case 1.—The patient, a boy 6 years old, had complained of pain and limp in the right foot for 6 months prior to admission to the Mayo Clinic. One month after the onset of the pain the child was taken to a physician. Roentgenograms were made and were reported to show nothing abnormal. The pain continued, and 4 months after its onset the child began to have a fever. Five months after onset of the pain, another roentgenogram was taken and the condition was interpreted as being tuberculosis. A cast was applied, but pain and fever continued. Biopsy was then done and was reported to show a "small cell sarcoma."

When examined, the lad looked pale and chronically ill. The right tarsal region was diffusely swollen and there was a recent wound due to biopsy. Results of general examination otherwise were normal. The sedimentation rate was 97 mm. in one hour. The concentration of hemoglobin was 10.6 Gm. per 100 cc. of blood. The erythrocyte count was 3,900,000, and the leukocyte count was 2100 per cubic millimeter of blood, of which 42 per cent were lymphocytes. A special blood smear showed large pathologic lymphocytes. This finding was confirmed by biopsy of the bone marrow. The roentgenogram of the thorax was negative; that of the foot showed an osteolytic process in the astragalus (Fig. 1).



FIG. 1

FIG. 1.—(Case 1) Involvement of astragalus of a boy, 6 years old, by osteolytic process. Diagnosis: lymphatic leukemia.

FIG. 2.—(Case 2) Ewing's tumor, grade 4, in leg of a boy, 6 years old. Condition was diagnosed as osteomyelitis before biopsy.



FIG. 2

The hematologist made a diagnosis of lymphatic leukemia. The pathologist's diagnosis on further examination of the tumor tissue was lymphocytic myeloma.

If the leukocyte count had not been made and found to be abnormally low, and this lead had not been pursued, an amputation for bone sarcoma would have been performed. This operation would have been needless, in view of the fact that the process was a general one and no cure could be anticipated. Instead of amputation the child was treated with urethane and with roentgen rays to the lesion, and the parents were advised that the prognosis was hopeless.

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CLASSIFICATION OF PRIMARY MALIGNANT BONE TUMORS

Many rather involved classifications of bone tumors have been proposed. The following list is of value because of its relative simplicity. It is a good working classification for the clinician and surgeon. It leaves out such rare and controversial tumors as liposarcoma and lymphangiosarcoma.

1. Osteogenic sarcoma
2. Fibrosarcoma
3. Chondrosarcoma
4. Ewing's tumor (or hemangio-endothelioma)
5. Multiple myeloma
6. Malignant giant-cell tumor
7. Reticulum-cell sarcoma

No attempt will be made here to distinguish the various types of primary malignant bone tumors, as they all present a different picture. I should like, however, in the following portion of this paper to distinguish these malignant bone tumors from other conditions which often simulate them.

DIFFERENTIATION FROM INFLAMMATORY LESIONS

Many bone tumors appear to be inflammatory processes. The differentiation between osteomyelitis and a primary bone tumor, especially Ewing's tumor, has always been a problem. This problem has become even more difficult to solve since the advent of the antibiotics, for now the classical picture of osteomyelitis is seldom seen. The picture is altered by penicillin, or one of the other antibiotics. As a result the clinical and roentgenographic findings are frequently difficult to interpret. As mentioned previously, all our diagnostic facilities must be used. Osteomyelitis and bone tumor frequently occur in young persons. In many cases the roentgenograms cannot be interpreted accurately and therefore too much reliance should not be placed on this measure in making the diagnosis. If roentgenograms are relied on completely, too many sad mistakes will be made.

Fever is not a common sign of most bone tumors but is a frequent sign of Ewing's tumor. It is also a prominent finding in fibrosarcoma of soft tissues. Many patients with Ewing's tumor present the clinical picture of an acute infection with fever, leukocytosis, local warmth and diffuse swelling suggestive of cellulitis or formation of an abscess. The sedimentation rate is usually elevated in these cases, but the leukocyte count does not usually rise as high in the presence of Ewing's tumor as it does in the presence of an infection. If any question remains as to diagnosis, two methods may be used to differentiate Ewing's tumor from osteomyelitis. A preliminary trial course of penicillin may be given and the response noted. Better yet, however, biopsy can be done, which will reveal the true nature of the lesion. Case 2 illustrates the confusion which exists between the diagnosis of Ewing's tumor and osteomyelitis.

Case 2.—The patient, a boy 6 years old, was known to have had diabetes for 18 months prior to examination. He was admitted to the clinic because of pain, swelling and warmth in the calf of the right leg of 10 weeks' duration. His first symptom was pain of the right calf, which came on rather gradually. Two days after the onset of the pain, the parents noted slight swelling in the calf of the right leg, and warmth of the skin over the swelling. When the child was first seen by his local physician, the picture was that of cellulitis of the calf and he was given penicillin. Roentgenograms were taken of the leg every other day for two weeks. The child then was taken to a chiropractor by his parents. The chiropractor manipulated his back but apparently did not rub the portion of the leg which was painful. The mother thought that the boy had been running a low grade of fever.

Examination on admission revealed a frail, poorly nourished, rather pale boy, 6 years old. The rectal temperature was 100.8°F. The upper third of the right leg was diffusely swollen, and local warmth and slight redness were present. The veins over the swelling seemed somewhat engorged. The right inguinal nodes were slightly enlarged. The impression of the initial examining physician at the clinic was that the patient was suffering from chronic osteomyelitis of the right tibia.

Laboratory findings showed a sedimentation rate of 34 mm. in one hour, 13.7 Gm. of hemoglobin, a negative flocculation reaction for syphilis, a fasting blood sugar of 56 mg., and a leukocyte count of 9400, with a normal differential count. A roentgenogram of the thorax revealed nothing significant; that of the tibia was interpreted by the roentgenologist as showing "chronic osteomyelitis of the right tibia with sclerosis of the proximal portion of the bone." He added: "There are islands of increased density, probably representing sequestra, and diffuse periosteal reaction of the upper two thirds of the shaft with concomitant soft tissue swelling" (Fig. 2).

Biopsy was advised because of some inconsistencies in the findings. A generous incision over the point of greatest mass was made. The subcutaneous fat and underlying tissues looked normal. When the raised periosteum over the tibia was incised a large amount of inspissated, white, purulent looking fluid escaped. Examination of this fluid failed to show pus cells. Biopsy of the tissue directly over the bone revealed a hemangio-endothelioma, grade 4, (Broders' classification) or Ewing's tumor.

This boy was treated with roentgen rays. Metastasis to the mandible and sacrum has occurred since the diagnosis was made.

Three findings in this case did not fit entirely into the picture of osteomyelitis: (1) the leg was more swollen and felt firmer than in the average case of osteomyelitis; (2) there was only a low-grade fever, and there was not much elevation in the leukocyte count; and (3) the roentgenographic findings could well be representative of Ewing's tumor, as well as of chronic osteomyelitis, which had been treated with penicillin. It is of interest also that even grossly, at time of operation, the condition looked much like osteomyelitis. The white, milky fluid, which is the result of cellular breakdown and is a frequent finding in Ewing's tumor, looked like inspissated pus, and I was not certain of the diagnosis until the pathologist gave me his report.

DIFFERENTIATION FROM TRAUMATIC LESIONS

Two traumatic lesions which may be confused with bone tumors are: (1) march or stress fracture; and (2) subperiosteal hematoma. In the differential diagnosis of traumatic lesions from lesions due to bone tumor must be included also the differentiation of a fracture due to trauma and a pathologic fracture due to bone tumor.

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March or stress fracture may occur in any of the long bones of the body, but usually is seen in the metatarsals. Case 3 illustrates the problems involved in the differential diagnosis between this type of fracture, with its fusiform enlargement of the bone and "onion skin" reaction of the periosteum, and a true bone tumor.

Case 3.—This patient, a girl 6 years old, was well until 6 months before admission, when she began complaining of mild pain in the right leg. Four months later she was taken to the physician in her home locality. He made a diagnosis of bone tumor and excised the lesion from the tibia. The pathologist in the home locality reported that the lesion was a chondrosarcoma.

Examination at the clinic revealed the operative incision and the postoperative roentgenographic appearance shown in Figure 3. Results of all other tests were within normal limits. A second biopsy was recommended to establish the grade of the tumor and therefore to help in the determination of the treatment. This was done and our pathologist reported that the lesion was a myxochondrosarcoma, grade 1. In view of the low grade of the tumor and no obvious evidence of metastasis, a wide local resection was carried out at the same time that the specimen was removed for biopsy, and the resulting defect was packed with bone chips from the bone bank (Fig. 4).

Ten months following this operation the patient returned for a postoperative examination. There was no pain or swelling in the right leg. There was no local adenopathy. Roentgenograms showed that the bone grafts were uniting and there was no evidence of tumor. There was, however, evidence of a fusiform swelling in the lower third of the fibula on the right side, with an area of rarefaction in the center (Fig. 5). My immediate reaction was that this represented either another primary tumor or a metastatic lesion. The mother was questioned further, and she then stated that 3 months previously the girl had fallen, and after this some swelling in this region had been present for 2 or 3 weeks. She stated that roentgenograms taken two days after the injury were reported negative.

The fibular lesion was a march-type of fracture which usually does not become evident in the roentgenogram for some weeks after the injury. The rarefied area in the center was absorption along the line of fracture and the swelling was the normal reaction of healing.

Another case, illustrating the difficulty in differentiating between traumatic and neoplastic lesions follows:

Case 4.—This patient, a boy 15 years old, presented the chief complaint of swelling of the left fifth finger. He stated that a year and a half previously he had injured his left hand severely in a football game, after which it became swollen. Roentgenograms were negative at that time. A small lump in the proximal phalanx of the left fifth finger persisted however, but remained asymptomatic until December, 1947, when it began to grow and became painful. Two months later this lump was excised and it was reported to be a "fibrous tumor." About 3 weeks after excision swelling seemed to occur rapidly, and the finger increased in size for about 5 days, and then stopped enlarging.

Our examination revealed a diffuse swelling of the left fifth finger with slight local warmth and tenderness. An operative scar was visible over the lateral aspect. There were no palpable lymph nodes and the laboratory findings were completely normal. Roentgenographic appearance of the finger was compatible with sarcoma (Fig. 6a and b).

It was decided that biopsy should be done, and a specimen was removed from a bloodless field. Then careful dissection of the entire tumor mass was carried out. It appeared grossly to be partly cartilaginous, partly bony, and partly fibrous. It extended down to

FIG. 3

FIG. 4



FIG. 5

FIG. 6

FIG. 3.—(Case 3) The patient, a girl 6 years old. Appearance of tibia after biopsy. Diagnosis: myxochondrosarcoma, grade I.

FIG. 4.—(Case 3) Three weeks after wide resection for myxochondrosarcoma, grade I, and bone grafting.

FIG. 5.—(Case 3) Ten months after bone grafting. Arrow points to healing stress fracture of fibula.

FIG. 6.—(a and b—Case 4) Swelling of the fifth finger of a boy, 15 years old, following injury, then biopsy. Roentgenogram compatible with diagnosis of sarcoma, but actually traumatic osteitis and periostitis was present.

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the periosteum. The tissue was thoroughly and carefully examined by our pathologist, who stated that it showed chronic osteitis and periostitis, and that areas of hemorrhage with nests of giant cells were present. He considered that possibly the etiologic factor was trauma. The wound healed without incident.

When the patient was examined 5 weeks later, the finger was normal in size, the wound was well healed, and the function in the finger was normal. Roentgenograms showed bony filling-in along the areas of the previously injured periosteum with no indication of any new growth (Fig. 7).

Further roentgenograms were reviewed 6 months later and showed nothing abnormal.

The lesion in this case represented a post-traumatic tumor which actually was an overgrowth of the normal healing process. The stimulus for this growth was the removal of the post-traumatic fibroma. Nevertheless, this finger was watched carefully postoperatively because of the peculiar nature of the lesion.

The third condition which must be differentiated in any discussion of traumatic lesions is that of pathologic fracture. Any bone tumor may result in a pathologic fracture, and the pathologic nature of these fractures is sometimes very difficult to determine. Fractures of the spinal column are in one of the most difficult regions in which to make the differentiation, because there the overlying soft tissues somewhat cloud the picture, and compression fractures from osteoporosis and relatively minor trauma are not uncommon.

Multiple myeloma is prone to attack the vertebrae. In fact, any severe backache in a middle aged or older person must be considered of myelomatous origin until proved otherwise. Multiple myeloma is the outstanding exception to the statement that primary malignant bone tumors occur among young persons. The average age at which multiple myeloma develops is between 50 and 55 years. As in other bone tumors, pain is a common symptom, and in a majority



FIG. 7.—(Case 4) Same finger as in Figure 6 after biopsy and operative resection. Diagnosis: traumatic osteitis and periostitis.

of the cases at the Mayo Clinic reviewed by Ghormley and Pollock,⁴ this pain was in the back. Case 5 illustrates the problem involved.

Case 5.—The patient, a nurse 64 years old, had been seen many times at the clinic since 1931 for various conditions, none of which apparently were related to her chief complaint of pain in the back on the admission under consideration. She stated that backache had been present for two and a half months prior to her present admission and that it followed the lifting of a bedridden patient. The pain was originally a knife-like twinge in the upper part of the lumbar region which did not extend into either extremity.

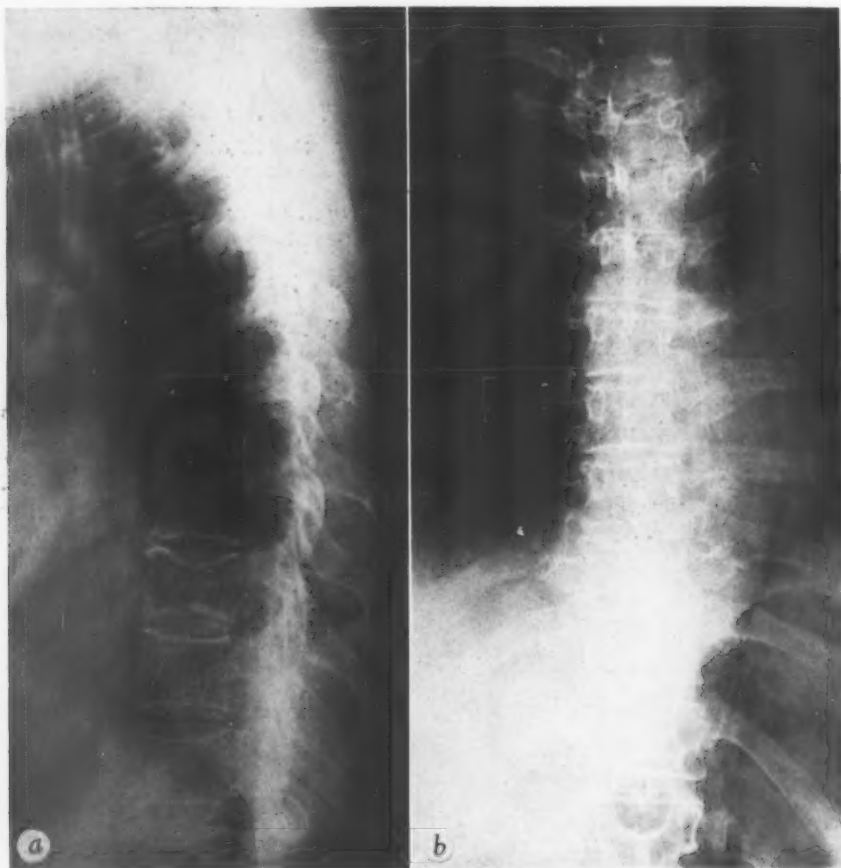


FIG. 8.—(a and b—Case 5) Patient, a woman 64 years old, with pathologic fracture of ninth thoracic vertebral body. Diagnosis: multiple myeloma.

Examination revealed a healthy-appearing woman of stated age. Temperature, pulse rate and respiration were normal. The general physical examination revealed nothing abnormal except tenderness to percussion low in the thoracic and high in the lumbar regions. Percussion in this area caused some extension of pain into the right side of the abdomen. This pain was so severe that the patient could not move in bed without crying out. Neurologic examination was undertaken because root pain was suspected, but the findings were normal.

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Roentgenographic examination of the back showed generalized osteoporosis, grade 1, of the spinal column, with slight osteo-arthritic lipping and in addition, a slight compression fracture of the ninth thoracic vertebral body (Fig. 8a and b).

The sedimentation rate was 85 mm. in one hour, and because of this, pathologic fracture was suspected. Further laboratory studies revealed a concentration of alkaline phosphatase of 5.2 Bodansky units. The value for total serum proteins was 7.8 Gm. per 100 cc., for albumin 4.1 Gm., and for globulin 3.7 Gm. The urine contained albumin, grade 1, with no Bence Jones protein. A special blood smear revealed normal morphology. The concentration of hemoglobin was 12.1 Gm. and the erythrocyte count was 3,950,000. A flocculation test was negative for syphilis and a roentgenogram of the thorax showed normal conditions. A roentgenogram of the skull revealed numerous destructive areas in the calvarium which were consistent with a diagnosis of multiple myeloma (Fig. 9).

On biopsy the bone marrow also presented the picture of multiple myeloma.



FIG. 9.—(Case 5) Appearance of skull. Diagnosis: multiple myeloma. Figure 8 also should be noted.

The diagnosis of multiple myeloma could not be made from the roentgenographic appearance of the spinal column alone. The presence of a pathologic fracture was suspected because of the elevated sedimentation rate, and the rather excessive pain from minimal inciting trauma. There was no Bence Jones protein. This protein is present in only 50 per cent of the cases of multiple myeloma reviewed by Bayrd and Heck.⁵ The findings on sternal biopsy were positive, as they are in more than 95 per cent of cases of multiple myeloma. The single best method of making the diagnosis short of biopsy of the actual bony lesion itself, is biopsy of the bone marrow.

SUMMARY

Advance in the knowledge of bone tumors in the past ten years can be attributed to (1) increasing understanding of the subject of tumor cytology and its value when this knowledge is used in conjunction with needle biopsy; (2) the application of Broders' grading of malignancy to bone tumors; (3)

further microscopic differentiation of tumors, such as osteoid osteoma, eosinophilic granuloma and reticulum-cell sarcoma, (4) the use of biopsy of bone marrow and (5) the development of the test to determine the sedimentation rate of erythrocytes and interpretation of results.

Malignant bone tumors are found chiefly in the younger age groups. Plans for mass detection of cancer, therefore, must emphasize this age group.

Pain is the important symptom of bone tumors.

Diagnosis of bone tumors is often difficult, and diagnosis from roentgenographic findings only is unreliable. *All* factors must be considered, including a careful history, complete physical examination, essential laboratory studies, roentgenograms and most important, surgical biopsy.

Biopsy itself is not 100 per cent accurate for the following reasons: (1) the tumor may have been treated previously by irradiation, and this may have caused some change in the structure and appearance of the cells; (2) previous removal of a specimen for biopsy may have resulted in infection, hemorrhage, or both which may confuse the microscopic picture; (3) the surgeon may not have taken a representative section of the tumor, or may miss the main substance entirely; (4) the pathologist may incorrectly interpret the tissue given him.

Besides differentiation of bone tumors from themselves, both benign and malignant, they must be distinguished from infectious and traumatic lesions of bone. Cases illustrating this point are presented. In Case 1 the differential diagnosis was made between a bone sarcoma as a purely localized lesion, and a generalized disease, in this case lymphatic leukemia, causing a local lesion. Treatment hinged on this important point. In Case 2 the difficulty was in differentiating osteomyelitis from Ewing's tumor. Case 3 illustrated the results of treatment of myxofibrosarcoma, grade 1. In this case also, an osteogenic sarcoma was differentiated from a stress fracture. In Case 4 the difficulty in diagnosis was in distinguishing between osteogenic sarcoma and a traumatic lesion, in this case periostitis. In Case 5 the differential diagnosis of pathologic fractures was involved, in this case, fracture due to senile osteoporosis versus fracture due to multiple myeloma.

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ACUTE VOLVULUS OF SMALL INTESTINE

ANALYSIS OF 36 CASES*

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TORSION OF A LOOP of small bowel sufficient to produce intestinal obstruction and circulatory embarrassment of the involved intestine is one of the most serious intra-abdominal catastrophes. Fortunately this is an infrequent occurrence, but when it does take place, the necessity of recognizing its development and of instituting proper therapy cannot be emphasized too strongly. This condition is always associated with some degree of small bowel obstruction, the signs and symptoms of which frequently overshadow those of the volvulus itself, making early diagnosis difficult. The mortality rate associated with this catastrophe indicates its importance. Few conditions which develop within the abdominal cavity end fatally so frequently, due primarily to the difficulty in early diagnosis, since the surgical treatment after recognition is not particularly difficult. The chief problem is to differentiate between those causes of obstruction which demand early surgery and those which can be treated conservatively. If operations were performed more frequently in those patients in whom the presence of strangulated bowel cannot be ruled out, there would be fewer deaths from the more conservative treatment now in vogue.

The basis of this study is an analysis of 36 cases of volvulus of the small bowel occurring at Strong Memorial Hospital and Rochester Municipal Hospital between 1925 and June 1947.

INCIDENCE

Sweet¹ analyzed the 520 cases of acute intestinal obstruction exclusive of strangulated external herniae occurring at the Massachusetts General Hospital from 1873 to 1930 and found that volvulus of small and large bowel accounted for 53 of these, or 10 per cent. Of this number, 36 (67.9 per cent) involved small bowel, ten (18.8 per cent) involved the sigmoid and in six (11.3 per cent) the cecum was the offending site. Of a total of 148 cases of bowel obstruction reported by Skjold² there were only six instances of volvulus of the small and large intestine. Of the 261,024 patients seen in the Strong Memorial Hospital and Rochester Municipal Hospital between 1925 and June, 1947, there were 36 cases of volvulus of the small bowel, an incidence of one in approximately 7500 patients.

No age group is immune to this condition, the youngest in this series being two days old and the oldest, 79 years. Only five patients were under 20 years

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of age, however, while 11 patients were over 60 years of age. The average age was 45 years.

PATHOLOGY

The pathologic changes which take place in the loop of bowel involved in a volvulus depend largely upon the degree of embarrassment to the circulation to that loop. At the neck of the volvulus the afferent and efferent loops of bowel are twisted upon each other and upon the mesentery to the loop. The degree of obstruction to the blood supply, therefore, depends upon the tightness of the twist in addition to the number of twists.³ The venous return is blocked by lower pressure on the veins than is necessary to occlude the arterial blood supply. Therefore, with a fairly loose twisting at the base of the volvulus, venous engorgement of the involved loop may result without significant decrease in arterial blood supply. When the twists tighten by further torsion or by edema, the arterial blood supply is also impaired. Not infrequently the vessels may be thrombosed because of damage to their walls and to stasis.

There is always some degree of intestinal obstruction in addition to the circulatory changes in the loop of bowel. The obstruction is due to occlusion of the loop at the point of twisting. The dilatation of the volvulus is probably due to the gas-forming organisms trapped within the loop and to transudation of fluid. It represents a closed loop obstruction in itself. In some cases, the proximal loop may not be completely obstructed. In this situation one might expect a greater dilatation of the volvulus and perhaps an earlier rupture of the bowel wall.

In 27 patients, the obstruction was apparently complete or practically complete, while nine patients were only partially obstructed. The specific location of the volvulus in the small bowel was not recorded in eight cases. Among the other 28 patients, the ileum alone was the affected site in 24 (85.7 per cent); the jejunum alone in three (10.7 per cent), and both ileum and jejunum in one case (3.6 per cent).

Circulatory changes in the loops were present to varying degrees. Sixteen of these cases showed irreversible circulatory changes with gangrene of the bowel wall. In one of these there was gross perforation of the bowel. In nine patients there were marked circulatory changes, which showed improvement with release of the volvulus and therefore did not require resection. In the remaining 11 cases, the circulatory changes were either absent or present to only a very slight to moderate degree.

ETIOLOGY

Volvulus of the small bowel rarely occurs in an otherwise normal abdominal cavity. Usually there is some congenital or acquired abnormality which predisposes to this condition. Fixation of a part of the bowel by an adhesion, congenital band or other congenital anomaly, provides a point about which the small intestine may twist. Incomplete developmental rotation of the bowel may result in an unusually long mesentery, allowing abnormal mobility of a loop,

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hence a greater chance to develop volvulus. Dott⁴ included volvulus in his discussion of the results of the arrest of development in any of the three stages of rotation of the intestines.

Our series contains several patients in whom the volvulus could be ascribed definitely to congenital malformation of the gastro-intestinal tract. One of them is of considerable interest and probably represents the youngest patient on record who survived resection of a perforated loop of intestine.

Case 1.—Baby boy C (261024) was born by hysterotomy in Strong Memorial Hospital on March 7, 1947, at 9:45 A.M. (Expected date of confinement March 29). The baby weighed 3070 Gm. at birth and appeared to be a normal healthy child. He took his feedings well and passed normal meconium per rectum shortly after delivery. On the morning of March 9 abdominal distention and lethargy were noted. No stools had been passed during the preceding day. Abdominal distention increased and the baby cried almost continuously.

Examination on the second day after birth revealed a small but well developed infant who appeared critically ill. The temperature was 37.8°C. (rectal) and blood leukocytes were 4600, of which 56 per cent were neutrophils. The abdomen was greatly distended and tympanitic. No peristaltic sounds could be heard. The liver dullness was obliterated. No masses could be felt in the abdomen. There was a soft mass in the left scrotum which was thought to be an indirect inguinal hernia containing a loop of bowel.

It was thought that the patient had intestinal obstruction, probably due to strangulated hernia with a perforation in the bowel at the point of strangulation. Roentgenogram of the abdomen revealed both free air and free fluid within the abdominal cavity (See Fig. 1).

Under ether anesthesia left rectus incision was made. A large amount of air escaped. There was much bile-stained fluid in the abdomen. The inguinal hernia had reduced itself prior to operation. The cecum lay in the right upper quadrant. There was a volvulus of 15 cm. of the ileum 12 cm. from the ileocecal valve. The intestine proximal to the volvulus was markedly dilated. The volvulus was twisted counterclockwise about 360° around a congenital fibrous band running from the liver down to the right lower quadrant. The involved loop appeared deep red at its base but was black and necrotic immediately adjacent to a hole in its midportion. The mesentery to the bowel involved in the volvulus was about one-third longer than the remaining mesentery. The congenital band was severed and the involved loop resected. End-to-end anastomosis was effected with 6-0

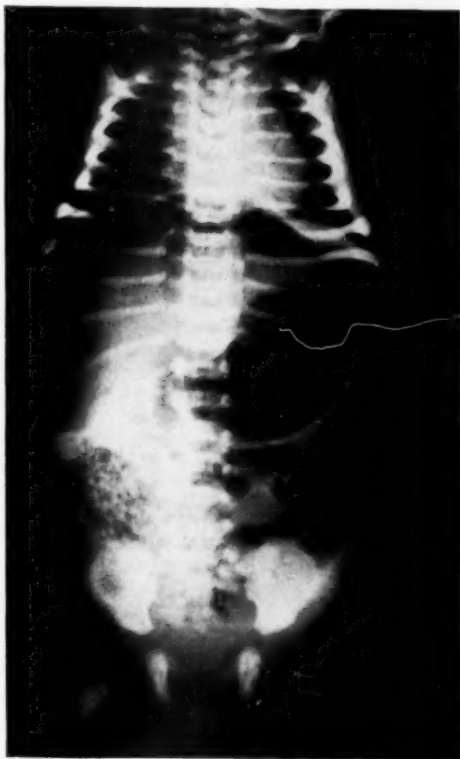


FIG. 1.—Roentgenogram of abdomen of 52-hour-old infant. A large amount of free air can be seen in the right upper quadrant extending to the left side between the liver and the diaphragm. Elsewhere there is a diffuse haziness denoting fluid within the peritoneal cavity.

silk. The patient's condition was extremely poor throughout the operation and remained critical for a week. He received continuous oxygen therapy, multiple blood transfusions, parenteral fluids and penicillin. His first stool was passed six days after operation. Brawny induration, present over the lower abdominal wall, back and thighs during the first ten days, finally subsided. Jaundice disappeared slowly. He improved gradually and was finally discharged about 4 weeks after operation. He was gaining weight and progressing satisfactorily when last seen 3 months later.

Buckley and Wells⁵ reported five cases of volvulus in the newborn, confirmed at autopsy.

In 20 patients with disturbances of developmental rotation of the intestine reported by McIntosh and Donovan,⁶ six had volvulus of a part of the intestine derived from the midgut. One of these was associated with atresia of the ileum; one was associated with malrotation and situs inversus abdominalis parietalis; and three were associated with obstruction of the duodenum by persistent peritoneal bands. The youngest surviving patient in this group was operated on when five days old and did not require resection of the involved bowel.

The importance of postoperative adhesions in the etiology of volvulus is emphasized by our experience. Twenty-five patients (69 per cent) had one or more previous laparotomies and, in 23 of these, an earlier operation was almost certainly responsible for the development of volvulus. In 21 of these 23 cases the cause was adhesions, while volvulus occurred about a colostomy and an enterostomy in the others. The average interval between the last preceding operation and the onset of volvulus was approximately seven years. Two patients developed volvulus within 15 days after operation.

It is of interest that 18 of these patients had no obstructive symptoms prior to the onset of volvulus. There had been bouts of abdominal pain suggesting partial small bowel obstruction in seven patients. Two of them had symptoms that suggested an earlier volvulus that had subsided.

Eleven cases had no previous laparotomy. Seven of these had fibrous bands, probably congenital, which were thought to be the cause of the volvulus. The fibrous band extended from the tip of a Meckel's diverticulum to the anterior abdominal wall in two of them. Small bowel volvulus in one patient had occurred about the base of a volvulus of the sigmoid. No abnormality to account for the volvulus was found in the other three patients.

Fourteen of the 37 cases reported by McKechnie and Priestley⁸ had previous operation, and in 21 cases peritoneal adhesions were found to be the predisposing cause. Eight of their cases had congenital anomalies, while 26 had some acquired predisposing cause. No demonstrable cause was found in three instances.

Kohn *et al.*⁷ were able to find in the literature reports of 76 cases of volvulus complicating pregnancy and they added two of their own. Nineteen of these involved the small intestine. One of our patients developed volvulus during the eighth month of pregnancy and is reported here because of the apparent rarity of this association.

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Case 2.—S. S. (183288) A 23-year-old white woman was admitted to Rochester Municipal Hospital May 20, 1942. On the morning of admission she developed severe crampy generalized abdominal pain. This shifted to the right upper quadrant, became constant, and radiated to the right back area. It was associated with nausea and vomiting.

She had an appendectomy 7 years before admission and 2 years before admission had an episode of intestinal obstruction which required operation for release of adhesions. She was known to have diverticulitis of the sigmoid colon and rheumatic heart disease, with mitral stenosis and insufficiency. Three months before admission she had a similar acute episode of abdominal pain, nausea and vomiting. At that time her leukocyte count was 23,000. Her symptoms subsided after a few days of expectant treatment.

The patient appeared acutely ill and moderately dehydrated on admission—T 37° C., P 90, R 20. Abdominal examination revealed marked tenderness in the epigastrium with referred rebound tenderness to this area. No peristaltic sounds could be heard. Roentgenograms were not obtained.

TABLE I.—*Characteristics of Abdominal Pain Recorded in 32 Patients with Volvulus of Small Intestine.*

Severity		Character		Localization	
	Per No. Cent		Per No. Cent		Per No. Cent
Severe.....	22 68.8	Cramplike.....	25 78.1	Generalized.....	4 12.5
				(without further localization)	
Moderate.....	3 9.4	Not cramplike.....	5 15.6	Upper abdominal.....	14 43.8
				Epigastric.....	13
				R.U.Q.....	1
Severity not stated	7 21.8	Character not stated	2 6.3	Para-umbilical.....	8 25.0
				Lower abdominal.....	5 15.6
				R.L.Q.....	1
				Lower abdominal.....	4
				(without further localization)	
				Localization not stated.....	1 3.1
Total.....	32		32		32

She was given intravenous fluids and Wangensteen suction but failed to improve. At operation on the day after admission a 12-inch segment of ileum was found to be gangrenous and twisted about an adhesion attaching the apex of the volvulus to the anterior abdominal wall. The involved loop of ileum was resected and an end-to-end anastomosis carried out. Corpus luteum hormone had been given the patient prior to operation but 5 hours postoperatively she delivered a stillborn child. Her convalescence was otherwise uneventful and she was discharged from the hospital on her sixteenth postoperative day. Two days later she was re-admitted with abdominal pain which subsided after a short period of decompression. She subsequently became pregnant again and gave birth to a normal infant. There have been no further symptoms of intestinal obstruction.

PREOPERATIVE DIAGNOSIS

No preoperative diagnosis was recorded in eight cases. Of the remaining 28 cases, the diagnosis of small bowel obstruction was made in 17 instances (47.2

per cent). The diagnosis of volvulus was made correctly in seven. Among the wrong diagnoses were mesenteric thrombosis, abdominal abscess, large bowel obstruction, acute appendicitis, gastro-intestinal cancer, intra-abdominal hemorrhage, perforated duodenal ulcer, acute gallbladder disease, and twisted ovarian cyst.

In patients seen relatively late, the diagnosis of intestinal obstruction was usually obvious, whereas the cause of the obstruction was obscure. In those seen shortly after onset of initial pain the problem was more that of a differential diagnosis of the acute abdomen and clinical intestinal obstruction frequently had not yet developed.

Symptoms. The pain of which the patients complained varied in localization, severity and character.

From Table I it can be seen that the majority of the patients had severe cramplike upper abdominal or para-umbilical pain.

Nausea and vomiting were usually prominent features of the history. Only two patients had neither of these symptoms. Vomitus was "fecal" or very foul in seven cases.

Diarrhea was a prominent symptom in only one patient. Fourteen patients had some degree of constipation ranging from no bowel movements in 24 hours in six patients to none in six days for one patient.

Only two patients had macroscopic evidence of blood in their stools.

Signs. The most common findings on examination were tenderness and abdominal distention.

There was no typical site of tenderness in this group, the localization depending chiefly on the location of the involved loop of bowel and upon the state of viability of the loop. In the more advanced cases the presence of bloody fluid or peritonitis usually but not invariably led to generalized tenderness.

Tenderness, present in 31 patients, was generalized in 14 and localized in the remainder. All areas were represented in those showing localized tenderness. In four cases, no mention was made of tenderness, and in one case it was recorded as absent.

Distention was present in 25 and absent in six cases. It was marked in ten, moderate in ten and only slight in five cases.

The presence or absence of peristalsis was noted in only 21 cases. There was marked increases in peristalsis up to borborygmus in 11 of these and only slight increase in one patient. Those in whom peristalsis was decreased or absent were the comparatively late cases as one would expect.

The degree of spasm present was somewhat surprising. Spasm was present in 12 and absent in 13 of the 25 in which a note was made regarding abdominal spasm.

Fluid within the abdominal cavity was noted on physical examination in only seven of these patients. However, an appreciable amount of ascitic fluid was present in 18 patients at operation.

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An abdominal mass was palpated in six patients; two in the left lower quadrant, two in the right lower quadrant, one in the left upper quadrant and one extending transversely across the mid-abdomen.

In the McKechnie and Priestley⁸ series, seven cases, including two of those with acute volvulus, had no significant abdominal findings on examination. Physical examination "commonly reveals distention, tenderness and rigidity." Pain was present in 85.7 per cent, nausea and vomiting in 74.3 per cent, constipation in 51.4 per cent and distention in only 11.4 per cent. The pain was colic-like in 45.7 per cent and steady in 37.2 per cent.

In the series reported by Leonard and Derow⁹ abdominal pain and vomiting were present in 100 per cent, constipation was present in 30 per cent and distention was present in 37 per cent. Abdominal tenderness and rigidity were found rarely in their series.

TABLE II.—Summary of Abdominal Signs in 36 Cases of Volvulus.

Sign	Number of Pts. With	Per Cent
I. Tenderness.....	31	86
Marked.....	11	
Moderate.....	14	
Slight.....	6	
Localization of tenderness		
Generalized.....	14	
Para-umbilical.....	3	
Upper abdominal.....	5	
Lower abdominal.....	10	
II. Distention.....	25	69
III. Peristalsis increased.....	12	
Decreased to absent.....	7	
IV. Spasm		
Present.....	12	33
Absent.....	13	
V. Peritoneal fluid		
Present by examination.....	7	
Present at operation.....	18	50
VI. Abdominal mass present on examination.....	6	
VII. X-ray film of abdomen.....	27	
Evidence of small bowel obstruction.....	19	70 (*)

* Percentage based on number of patients (27) who had roentgen ray film of abdomen taken.

Roentgenograms. A roentgenogram of the abdomen was taken in 27 patients. Nineteen of them showed evidence of small bowel obstruction; two showed evidence of large bowel obstruction; one showed free air in the right upper quadrant with evidence of fluid in the peritoneal cavity (Figure 1). The roentgenograms appeared normal in five patients.

A summary of the physical signs is presented in Table II.

Laboratory Findings and Vital Signs. In general, the temperature, pulse and respiration were of little value as indications of the pathologic condition within the abdomen. Only six patients had a temperature greater than 38°C. and in 12 patients the temperature was 37°C. or less. In those patients requiring bowel resection, the pulse rate averaged 110, but this too was unreliable.

The degree of leukocytosis roughly corresponded to the degree of strangulation of the involved loop of bowel in many cases. The average white blood count in the 31 cases in which these figures were available was 16,200. Of the 14 cases in which resection or exteriorization was obligatory, the average leukocyte count was 18,820. In those with operation not requiring resection the average was 14,600. Nineteen (61 per cent) of the 31 had at least a 14,000 white blood cell count. The highest count was 39,200 and the lowest was 4600. Certainly other factors, such as state of hydration, affect the total leukocytes, but in general the higher degrees of leukocytosis were associated with serious impairment of the circulation to the involved loops of bowel.

The discrepancy between our findings and the observation by McKechnie and Priestley⁸ that the "leukocyte count is usually approximately normal except in acute cases where it may be slightly elevated," may be explained by their unusually low (16 per cent) incidence of seriously impaired circulation in the affected loop. McKittrick and Sarris¹⁰ have stressed the importance of increasing leukocytosis in successive blood counts. They feel that this suggests strangulation of the intestine. Our observations support this thesis.

TABLE III.—*Relationship Between Type of Surgery and Mortality Rate.*

Operative Procedure	No. Cases	No. of Deaths	Mortality Rate
1. Release fibrous band with untwisting of volvulus.....	17	1	5.9%
2. Laparotomy—untwisted prior to operation.....	1	0	0
3. Resection with primary anastomosis.....	13	6	46.2%
4. Exteriorization with side-to-side entero-enterostomy	1	1	100 %
5. No operation for volvulus.....	4	4	100 %
Total.....	36	12	33.3%

Peritoneal Fluid. The presence of free fluid in the peritoneal cavity was noted at operation in 18 patients. This fluid was bloody in 11, frankly purulent in one and serous in six instances. Seven of 11 cases with bloody fluid required resection for non-viable bowel, while only two of the six cases with serous fluid required resection. One should suspect the presence of gangrenous loops of bowel in those with bloody fluid in the peritoneal cavity and elect early surgery.

Treatment and Prognosis. Our high mortality rate, 33.3 per cent, compares favorably with other reported series (Table III).

Leonard and Derow⁹ reported 16 cases of small bowel volvulus with nine deaths, a mortality rate of 56 per cent. Seven of these nine deaths followed more extensive surgery than simple untwisting. The five enterostomies and two resections in their series all ended fatally. Skjold² reports two deaths in six patients with volvulus, without stating whether or not these occurred in small bowel. McKechnie and Priestley⁸ reported 34 cases with six deaths, but only 21 of these cases were classified as acute volvulus of the small bowel. If, as seems probable, these six deaths occurred in acute volvulus, their mortality

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rate for acute volvulus would be 28.6 per cent. Michael,¹¹ in reporting 160 cases of obstruction not due to cancer, included 11 cases of volvulus. One of these patients died shortly after admission without surgical intervention, and the remaining ten were operated upon. Five cases survived simple release of adhesions and five cases died after other operative procedures.

Only one of our 18 cases requiring only release of adhesion with untwisting of the volvulus ended fatally. This death was due to coronary thrombosis. Certainly this is the best method of treatment when it suffices. However, when the loop is gangrenous, resection is necessary. Thirteen patients in our series required resection. Six of them died, all within three days of operation. Exteriorization with side-to-side anastomosis might have been tried but probably would not have altered the fatal outcome. This procedure was carried out in one case, but the patient succumbed within 24 hours. In one case laparotomy was performed and evidence of previous volvulus, which had already untwisted itself at time of operation, was found.

One hundred per cent mortality occurred in the group in which no operation was carried out for the volvulus. Two patients were seen too late and in too poor condition to stand surgery. In one case, surgery was directed at strangulated hernia without laparotomy. In the other, a mid-thigh amputation was done for gangrene but no laparotomy was done.

The relationship between the mortality rate and the duration of symptoms prior to operation is of particular interest. The average duration of illness before operation in 12 fatal cases was more than six days. In the 23 patients who survived, the average interval was less than two days. Only one case with symptoms over three and a half days survived, and only one case with symptoms less than 36 hours died. The patient who lived with symptoms over three and a half days had a six-day history of symptoms before admission and had partial relief with a Miller-Abbott tube. Four days after admission he was operated upon, at which time the bowel was not gangrenous. Its color returned to normal after release of fibrous band and no resection was necessary. The patient who died with symptoms of less than 36 hours developed a postoperative obstruction from a kinking of the bowel, requiring a second operation on the third postoperative day. He died two days later with generalized peritonitis.

Leonard and Derow⁹ noted that the average duration of symptoms in patients with volvulus of the small bowel before operation was 48 hours in nine fatal cases, while in the seven non-fatal cases the interval averaged 38 hours. They concluded that this delay of ten hours might have accounted for the fatalities.

The need for early operation is illustrated by one patient who was operated upon two hours after the onset of symptoms. A foot of ileum was found to be gangrenous and required resection. Dennis and Brown¹² stressed the importance of early operation in patients with obstruction of small bowel especially when signs of peritoneal irritation are present.

McKittrick and Sarris¹⁰ stressed the increased hazards of small bowel obstruction in old patients. In their series of acute intestinal obstruction of the small bowel from all causes, the mortality rate was 64 per cent in patients over 60 years of age. Eleven patients in our group were over 60 years of age and only three of these survived, a mortality rate of 72.7 per cent. Twenty-four patients under 60 years of age had a mortality rate of 16.4 per cent.

Improvement in our understanding of volvulus would be a cause for optimism. A comparison was made between the first 18 cases in this series, admitted prior to July 1, 1940, and the last 18 cases, admitted subsequent to that date.* In the first 18 cases there were eight deaths, while in the last 18 cases there were four deaths, with resulting mortality rates of 44 per cent before July, 1940, and 22 per cent after July, 1940. Most of the improvement was probably due to more adequate fluid replacement, blood transfusions, decompression by Miller-Abbott tube and chemotherapy. In the more recent group more patients entered the hospital promptly after the onset of symptoms and more were operated upon without delay. McKittrick and Sarris¹⁰ ascribe their recent improvement in results to the fact that more patients were operated on within 24 hours after the onset of symptoms. Our series is too small to be significant in this respect, but more prompt treatment appears to have been an important factor.

A study of the fatal cases is of interest. In only three of these patients was there any likelihood that death might have been prevented. Errors in diagnosis in each case led to delay in surgical treatment, thereby decreasing chance of survival.

One patient was observed on Medical service for three days before surgical consultation was sought. At operation generalized peritonitis was present. Gangrenous jejunum was resected and end-to-end anastomosis was performed. The patient died 24 hours later. Prompt surgical consultation and operation probably would have prevented this death.

Another patient was observed on Surgical service for 24 hours before operation. A tender mass was present on admission in the right lower quadrant and serous fluid was obtained by abdominal tap. Roentgen ray examination of abdomen showed no evidence of bowel obstruction. Delay in operation was justifiable, since a diagnosis of abdominal abscess was made. At operation 24 hours after admission, resection of two feet of small bowel was necessary. The patient died 40 hours later with peritonitis in spite of an intact anastomosis. Immediate laparotomy before onset of peritonitis might have been life-saving.

The third possibly preventable death was that of a 74-year-old woman who was admitted with partial large bowel obstruction due to carcinoma of sigmoid. A cecostomy done shortly after admission failed to relieve her symptoms. Two days later laparotomy revealed a gangrenous loop of jejunum and ileum twisted about the adhesions to a midline incision made many years before.

* These two groups are fairly comparable as to number resected (7:6); number untwisted (8:10); number not operated on (2:2); number exteriorized (1:0).

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Death occurred seven hours after resection of this gangrenous bowel, from cardiovascular collapse. Recognition and treatment of the volvulus at the time the cecostomy was performed might have prevented this fatality.

The other deaths were for all practical purposes unpreventable. Four were too late on admission; two probably developed the volvulus as a terminal event without causative relationship to the fatality, and three died because of some other uncontrollable factor.

DISCUSSION AND CONCLUSIONS

The chief difficulty lies in differentiating between the various causes of symptoms of small bowel obstruction, presented by most of these patients.

If the physical examination, history and laboratory findings suggest the probability of strangulation of bowel, then early operation is advisable, even if there is some improvement in condition with decompression. The presence of fluid, either on examination or tap, indicates need of operation.

In our experience we have seen no harm result from a diagnostic abdominal tap. We feel that this should be attempted in the doubtful cases. Within four hours after experimentally producing strangulation of loops of jejunum Hill *et al.*¹³ found that bloody fluid was present in the peritoneal cavity which could be aspirated. If free fluid is obtained, laparotomy should be advised. If the peritoneal fluid is bloody, operation is practically mandatory.

The presence of a tender mass in the abdomen associated with obstruction should demand exploration.

Marked leukocytosis, pulse elevation or fever beyond that expected from state of hydration should make one suspect strangulation of bowel.

Absence of spasm should not influence observer against diagnosis of volvulus. The presence of persisting tenderness almost anywhere in abdomen is in favor of volvulus or some other form of strangulating obstruction and should indicate exploration.

Wangensteen¹⁴ emphasizes the importance of tenderness in the presence of intestinal obstruction. When this is present on admission or when it develops in a patient whose findings are otherwise those of simple obstruction, he favors early operation.

McKittrick and Sarris,¹⁰ in an excellent presentation of small bowel obstruction, concluded that, because of the difficulty in differentiating between simple and strangulating obstruction, early operation is advisable in all cases of small bowel obstruction seen within 48 hours after onset of symptoms.

Most important is to make a determined effort to ascertain the presence or absence of volvulus or strangulation in all cases of small bowel obstruction. It will not suffice simply to diagnose small bowel obstruction and to start decompression from above. Careful observation must be continued and the possibility of the need for surgical intervention must be kept in mind. McKittrick and Sarris¹⁰ point out in their series of 136 cases of small bowel obstruction that if there was a delay of operation for six hours there was invariably a delay of

at least 24 hours, the average delay in this group being 48 hours. They recommend a twice daily leukocyte count in any patient being observed and believe that a rising count is of more significance than a single high or low determination.

The type of operation to be performed depends upon the conditions found when the abdomen is opened. If simple release of the adhesion with detorsion of the volvulus is all that is required then this is the procedure of choice. Frequently a markedly strangulated loop of bowel will give evidence of viability after release and application of warm packs to the loop of bowel. If after ten to 12 minutes, there is no evidence of the bowel being viable, or if there is serious doubt as to its viability, the preferred treatment is resection of the strangulated bowel with adequate margin and an end-to-end anastomosis. As demonstrated in this series of cases, most patients will tolerate this procedure quite well. In an extremely poor risk patient, exteriorization may be permissible. Gatch¹⁵ advocated this procedure with the establishment of a "gun barrel" enterostomy for those in whom there was great distention of the bowel, the anastomosis to be performed after recovery from the acute illness.

Dennis and Brown¹² have had considerable success in performing primary aseptic anastomosis in the presence of marked degrees of obstruction and gangrenous bowel. They stressed the benefits of local implantation of sulfathiazole in the emergency cases where preoperative succinyl sulfathiazole could not be given.

McKittrick and Sarris¹⁰ pointed out that it is not so much the magnitude of the operation that is responsible for the higher mortality where more extensive operations are required as the advanced stage of the disease and the associated complications such as peritonitis. Morton¹⁶ emphasizes the need for gentle handling of the tissues and for limiting the amount of surgery performed to that actually necessary to relieve the condition found at operation. Any added procedure is meddlesome surgery and adds an unnecessary risk. Orr¹⁷ stated that the briefest operation with the least possible trauma is the procedure of choice. He states that although enterostomy may be life saving and may be the only operative procedure necessary for bowel obstruction, it will not suffice where there is strangulation. One is impressed in reviewing the literature on this subject by the number of cases treated by enterostomy and the high percentage of deaths following this procedure.

Wangensteen¹⁴ states that primary resection of strangulated bowel with primary end-to-end anastomosis is to be preferred to an exteriorization operation.

The more adequate pre- and postoperative treatment with proper fluid replacement therapy has played an important part in decreasing the mortality from this condition. Sulfonamides and penicillin have aided greatly. The advent of the Miller-Abbott tube has aided considerably but is not without danger. The only way in which these results can be materially improved is by earlier diagnosis and earlier surgery.

SUMMARY

Thirty-six cases of acute volvulus of the small bowel occurring in the Strong Memorial Hospital and Rochester Municipal Hospital between 1925 and 1947 are analyzed.

A case history is presented of a 52-hour-old infant treated successfully by resection of the involved perforated loop of ileum with primary end-to-end anastomosis. Another case is presented of a volvulus occurring in a woman, seven months pregnant, treated successfully by resection and primary anastomosis.

Twenty-five (69.4 per cent) of these cases had had previous laparotomy, and in 28 (77.7 per cent) patients either acquired or congenital fibrous bands were thought to be the principal predisposing cause of volvulus.

The most frequent preoperative diagnosis was small bowel obstruction.

The usual symptoms were severe, cramplike, upper abdominal or para-umbilical pain associated with nausea and vomiting.

The usual signs included abdominal tenderness (86 per cent), and abdominal distention (69 per cent). Peristalsis ranged from absent (usually in the late cases) to hyperactive. Spasm of the abdominal muscles was present in only 12 of the 25 cases in which the presence or absence of spasm was recorded. Evidence of small bowel obstruction by roentgen ray was usual (70 per cent).

The average leukocyte count in those requiring removal of the bowel for gangrene was 18,800; in those in whom detorsion of the volvulus was all that was required the average was 14,600.

The mortality rate of this group of 36 patients with acute volvulus was 33.3 per cent.

In 18 cases no more extensive surgery than release of fibrous band and untwisting of the volvulus was necessary. Only one of this group died (5.5 per cent). In 14 cases either resection with end-to-end anastomosis (13) or exteriorization (1) was done. Seven (50 per cent) of this group died. In four cases, no surgery was performed for the volvulus and all four of these died.

Of considerable importance in the prognosis is the duration of symptoms prior to operation and the age of the patient. The average duration in the fatal cases was approximately six days, while in the non-fatal cases the average duration was less than two days. The mortality rate in those over 60 years of age was 72.7 per cent and in those under this age was 16.4 per cent. The mortality rate prior to July, 1940, (18 patients) was 44 per cent and after July, 1940, (18 patients) was 22 per cent.

Satisfactory treatment of this condition requires an early diagnosis. Diagnosis of the cause of the obstruction rather than simply the presence of intestinal obstruction is one of the chief difficulties encountered.

The proper surgical treatment depends upon the conditions found at operation. In general, the simplest procedure with the least trauma is best. Severing the constricting band and untwisting the volvulus suffices in many. If

the bowel wall is gangrenous, then resection with end-to-end anastomosis is advocated.

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DUODENAL FISTULA*

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IN 1938, BARTLETT AND LOWELL² reported 128 cases of duodenal fistula in what they considered to be a complete review of the literature from 1865 to 1937. We have found 18 cases reported since 1937^{1, 3-14} and are adding six cases treated at this hospital to bring the total to 24. We shall use these 24 cases as a text in discussing duodenal fistula.

ETIOLOGY

Duodenal fistula is most commonly encountered as a complication following right upper quadrant abdominal surgery. This was true in 23 of the 24 cases here reviewed. The mechanisms by which the fistula is produced at or following operation are varied and may be multiple. Accidental trauma to the duodenum during biliary surgery, right hemicolectomy, nephrectomy, etc., may lead to fistula formation. The fistula may result from failure to obtain and maintain a satisfactory closure of a perforation of the duodenum due to ulcer or other nonoperative trauma. This was the case in five (and possibly six) of the cases being reviewed. The most common single cause of this type of fistula was leakage from the duodenal stump following gastric resection (nine cases). Infection, impairment of blood supply, hematoma formation, poor nutrition, and improperly placed drains all may contribute to the development of a duodenal fistula. Table I lists the etiologic factors for the fistulas in the cases under discussion.

TABLE I.—*Etiologic Factors.*

	Number of Cases
1. Gastric resection ^{1, 5, 6, 8, 14}	9
2. Right nephrectomy ^{7, 10}	5
3. Perforated duodenal ulcer ^{4, 6, 12}	4
4. Biliary Tract Surgery ⁹	2
5. Right hemicolectomy.....	1
6. Right upper abdominal operation ¹¹	1
7. Incision and drainage, right subphrenic abscess ³	1
8. Right upper quadrant war wound ¹³	1

CLASSIFICATION

There are two types of duodenal fistulas; namely, the "end" type and the "lateral" type. The latter occurs with the bowel in continuity and the former

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in the duodenal stump usually following gastric resection. The "end" type fistula is less common, and at the same time less serious, than the "lateral" type, both as to morbidity and mortality. In the series reported by Bartlett and Lowell² only 14 of the 128 cases were of the "end" type. In the cases reviewed by us, nine of the 24 were of the "end" type. Undoubtedly, this increase in incidence of the "end" type fistula in later years is a reflection of the acceptance of radical gastric resection over lesser surgical procedures in the treatment of complicated duodenal ulcer. Table II compares "end" and "lateral" type fistulas with respect to frequency.

TABLE II.—*Fistula Classified.*

	Total	"End" Type	"Lateral" Type
Cases reported by Bartlett and Lowell . . .	128	11%	89%
Current series	24	37.5%	62.5%

DIAGNOSIS

As a rule the recognition of duodenal fistulas complicating surgical procedures on or about the duodenum is not difficult. If drainage was established primarily, the first sign of a fistula may be the appearance of watery, bile-stained fluid on the dressings, often in copious amounts. In undrained cases onset is heralded by epigastric or right upper quadrant pain. The wound may become inflamed and indurated, and open spontaneously to discharge duodenal content. On the other hand a deep intra-abdominal collection may form and require surgical drainage to reveal the true nature of the complication. Rarely is the picture that of spreading peritonitis.

When dye such as carmine or methylene blue is given by mouth, there is prompt appearance of the dye from the "lateral" type fistula. Gastro-intestinal barium studies may yield additional information as to size and location of the fistula.

TREATMENT

At the occurrence of a duodenal fistula, the care of the patient is complicated immeasurably. An excessive loss of fluid and electrolytes must be replaced. Adequate nutrition must be maintained. Every effort should be made to prevent or minimize the excoriation of the skin produced by the irritating secretions discharged from the fistula. Finally, operative closure of the fistula may be necessary if spontaneous closure does not result after a reasonable length of time.

Prompt therapy cannot be too strongly emphasized. As much as 4000 cc. of fluid may be lost through a duodenal fistula daily, and delay in restoring fluid and electrolyte balance may result in biochemical changes which are irreversible. Factors influencing the composition and amount of drainage are:

1. Type of fistula, "end" or "lateral."
2. Intake, both enteral and parenteral.
3. Location and size of the fistula.
4. The intraduodenal pressure.

In the "lateral" type fistula at or below the ampulla of Vater, there is loss of secretions of the stomach, duodenum, liver and pancreas. In "lateral" type fistulas located near the pylorus, there will be a relatively greater loss of stomach contents than pancreatic and liver secretions. The opposite occurs in "end" type fistulas with loss of pancreatic secretion and bile and little or no loss of the gastric juice. It is obvious therefore that the treatment of each patient must be individualized on the basis of the above considerations.

When feasible, the enteral route should be utilized to its fullest extent for fluid and electrolyte replacement and for maintenance of nutrition. In the presence of "end" type fistulas complicating gastric resection and associated with a functioning gastro-enterostomy, little recourse to parenteral therapy may be necessary. A well-balanced diet complete in mineral and accessory food factors may be given by mouth. However, the possibility of improper digestion and deficient absorption due to loss of bile and pancreatic juice from the fistula must be considered. Occasionally it is possible to collect and re-feed these secretions.

In dealing with "lateral" type fistulas, on the other hand, enteral feeding may not be feasible or beneficial and actually may be harmful. A goodly portion of the fluid and food taken by mouth may be lost through the fistula. In addition, the flow of gastric, biliary and pancreatic secretions through the fistula may be increased so markedly by mouth feeding that the net result, from the standpoint of intake-output ratio, is a loss rather than a gain. When a Miller-Abbott tube can be successfully passed beyond a "lateral" type duodenal fistula and into the upper jejunum (Cases 5 and 6) beneficial feeding may be accomplished through the tube. The passage of a feeding tube through the fistulous opening and into the distal bowel has been accomplished. However, this method of enteral feeding is undesirable because it retards or prevents spontaneous closure of the fistula.

The parenteral routes may be used to supplement enteral feeding. In some instances the problems of fluid and electrolyte replacement and maintenance of nutrition must be solved entirely by administration of parenteral fluids. Glucose in water, saline solution, plasma, serum albumin, protein hydrolysates and whole blood are used as indicated. Therapy in terms of type and amount of solution administered is controlled by accurate intake and output records, including estimation of loss through the fistula, daily weight charts, frequent blood chemistry estimations, and above all, evaluation of clinical response. Maintenance of an adequate daily urinary output, 1000 to 1500 cc., is the best clinical guide with respect to fluid requirements. Overloading the patient with saline solution is to be avoided. The necessity for potassium replacement, particularly during long periods of parenteral feeding, is to be considered.

Very occasionally, it is necessary to resort to operative methods for solving the feeding problem. Jejunostomy is the simplest of the procedures available and may be life saving in selected cases. Gastro-enterostomy with pyloric exclusion has been recommended to convert a "lateral" into an "end" type fistula and permit effectual mouth feeding.

Numerous methods have been proposed for care of the abdominal wall and for prevention of extensive skin erosion. A brief summary of these methods follows:

1. Inactivation of the pancreatic ferments, amylase and trypsin, by a calculation of the pH of the products of the fistula and converting to a pH which retards the action of these enzymes.
2. Prevention of contact of the discharge with the skin by applying ointments or pastes of various kinds.
3. Adsorption of the ferments by finely divided charcoal or kaolin.
4. Irrigation of the wound with peptone powder, proteins or beef juice for chemical neutralization of the ferments.
5. Mechanical removal of fluids either by intraduodenal suction or by a suction tube in the fistulous opening. The use of a combination of irrigation and suction has been recommended.

We have not used all of the protective methods outlined above and described more fully in the various articles reviewed. In our experience a combination of aluminum paste, suction on the wound, and frequent change of dressings has proved to be quite satisfactory in protecting the skin, especially if treatment is started before any erosion has taken place.

Finally, surgical closure of the fistula must be considered when after prolonged nonoperative treatment, spontaneous closure does not occur. Of the 24 cases being discussed only five were treated surgically. Three had jejunostomies for feeding purposes. In two of these, the fistula healed spontaneously, and one patient died. Two cases required surgical closure of the fistula.

MORTALITY

The death rate resulting from duodenal fistulas has been high. The overall mortality reported by Bartlett and Lowell was 37 per cent, while that in the current series was 16.6 per cent. The diminishing mortality rate is attributed to the relative decrease in frequency of "lateral" type fistulas and to the better understanding and treatment of the nutritional and chemical changes produced by a duodenal fistula.

Table III presents mortality statistics and illustrates the relative benignity of the "end" type as compared with the "lateral" type fistula.

TABLE III.—*Mortality.*

	"End" Type	"Lateral" Type
Cases reported by Bartlett and Lowell.....	14%	40%
Current series.....	0%	26.6%*

* Case 6 herein reported died with a "lateral" type fistula and is included in the mortality statistics. However, the fistula was not the primary cause of death.

Case 1.—J. B., a 41-year-old white male, was admitted to this hospital on June 18, 1946. His history, clinical and laboratory findings were those of a bleeding duodenal ulcer. He had had recurrent episodes of bleeding since his initial diagnosis of duodenal ulcer in 1941. Following admission, the patient seemed to respond satisfactorily to sup-

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portive therapy, until June 20, when an exsanguinating hemorrhage led to emergency operation, with transduodenal ligation of a large artery at the base of a posterior duodenal ulcer. Postoperative course was uneventful. A subtotal gastric resection was performed on July 31. Following this procedure, the patient bled profusely from the stomach via the Levin tube and vomiting. He was re-operated upon the same night and an actively bleeding vessel at the anastomosis was ligated. Postoperative course was complicated by a wound abscess which was drained of a large amount of foul-smelling, purulent material. On August 9, it was first noted that the discharge was bile-stained. Continuous mouth feedings, supplemented by intravenous fluids, blood and plasma, as indicated, resulted in satisfactory electrolyte and fluid balance. Suction was maintained on a catheter in the wound. The skin surrounding the wound was protected with aluminum paste. Drainage subsided and on August 14 the catheter was removed and the wound healed promptly. The patient was discharged from the hospital on September 26, 1946.

Factors which probably contributed to the formation of a duodenal fistula in this case were difficulty in obtaining a satisfactory closure of an indurated and edematous stump, hemorrhage, and sepsis.

Case 2.—J. L., a 54-year-old white male, was admitted to the hospital on August 23, 1947. The diagnosis of carcinoma, stomach, was established and on September 15, a subtotal gastric resection was performed. On September 24 there was a copious drainage of thin, bile-stained fluid from the wound. The patient was maintained on mouth feedings with supportive therapy of intravenous fluids, blood and plasma to maintain satisfactory electrolyte and fluid balance. The drainage slowly subsided, and by October 20 the fistula was closed. The skin was protected by means of aluminum paste and excoriation was minimal.

Case 3.—G. L., a 47-year-old white male, was admitted to the hospital on April 7, 1947, because of tarry stools and hematemesis. He had had perforated ulcers repaired in 1933 and in 1935. The diagnosis of bleeding posterior duodenal ulcer was made, and hemorrhage subsided on conservative measures. However, because of the multiple complications and intractability, a subtotal gastric resection was done on May 20, 1947. It was evident, on the sixth postoperative day, that the patient had a duodenal fistula. He was maintained on oral feedings and intravenous fluids to maintain satisfactory electrolyte and fluid balance. Skin around the fistulous opening was protected with aluminum paste. The fistula closed on August 11 and reopened on August 14 and continued to drain 500 to 1000 cc. daily. By October 23 it was apparent that the mucous membrane of the bowel was in continuity with the skin and that spontaneous closure was improbable. Surgical closure was performed with a good result.

Case 4.—T. M., a 59-year-old white male, was admitted to this hospital on December 29, 1947. After study, a diagnosis of obstructive jaundice due to stones in the common duct was made, and an operation performed on January 26, 1948. The gallbladder was found to be small and fibrotic, but contained no stones. Exploration failed to reveal stones in either the hepatic or the common ducts. Obstruction was thought, at that time, to have been due to inflammatory reaction at the junction of the cystic and common ducts. A T-tube was placed into the common duct and the gallbladder was removed. A Penrose drain was brought out of the wound from the foramen of Winslow. The postoperative course was relatively uneventful, except that the patient was apprehensive and cooperated poorly. On the tenth postoperative day he complained of right upper quadrant pain, radiating through to his back. A roentgenogram disclosed evidence of a right subphrenic abscess. This abscess was drained of bile-stained material on February 7, 1948. Convalescence was uneventful and the wound healed without difficulty. However, repeated cholangiograms revealed a stone at the lower end of the common duct. On March 19 the patient was again explored and a large stone removed from the common duct. During the operative procedure, there was considerable trauma to the duodenum and a small

devitalized area was noted on its anterior surface. This area was oversewn, but the formation of duodenal fistula was feared. The first few days were stormy, with the patient in critical condition. On the fifth postoperative day copious drainage of bile-stained material and marked skin irritation were noted. The patient was maintained on oral feedings, supplemented by intravenous fluid as necessary to maintain satisfactory electrolyte and fluid balance. Aluminum paste used on the skin was rather ineffectual because of the marked excoriation present when the diagnosis was made. The fistula closed spontaneously after 20 days.

Case 5.—H. M., a 40-year-old white male, entered the hospital on April 20, 1947, with history and clinical findings of a perforated peptic ulcer. Laparotomy was performed immediately and a perforated duodenal ulcer was closed. The right lateral gutter was drained. Postoperative course was febrile and there was profuse drainage from the wound. On the fourth postoperative day the drainage was noted to be bile-stained, and a duodenal fistula suspected. A Miller-Abbott tube was passed into the small bowel beyond this fistula. On the seventh postoperative day the drain was removed inadvisedly and drainage ceased. However, the patient developed signs of a right subdiaphragmatic abscess and on May 6 the right subphrenic area was drained through a subcostal incision. Profuse drainage of bile-stained fluid followed, and suction was instituted on the fistulous opening. The skin around the fistula was protected with aluminum paste. Treatment consisted of jejunal feedings through the Miller-Abbott tube, intravenous therapy of saline, glucose, blood, blood plasma and serum albumin, as necessary, to keep the patient in chemical balance. Drainage slowly subsided, and on May 27, 1947, suction was discontinued. Barium swallow showed no evidence of a fistulous tract. Oral feedings were begun and the patient improved uneventfully.

Successful passage of the Miller-Abbott tube beyond the fistula simplified treatment of the patient immeasurably. With the tube in the jejunum, re-feeding of the lost duodenal contents was possible. Aided by frequent blood chemistry studies, needs in supplementary parenteral fluids were readily estimated. A Levin tube in the duodenum connected to Wangenstein suction was used to minimize the intraduodenal pressure and loss of secretions through the fistula. External suction on the fistulous opening helped to prevent wide excoriation of the skin.

Case 6.—W. H. S., a 65-year-old white male, was operated upon for an obstructing carcinoma of the hepatic flexure of the colon on August 23, 1948. An undiagnosed and unsuspected large, retroperitoneal, retrocecal abscess was entered and evacuated of foul-smelling pus and liquid feces, which were escaping through necrotic posterior bowel wall. Right hemicolectomy progressed uneventfully to the point of mobilizing the primary lesion which extended into the duodenum. This latter structure was opened through carcinomatous tissue. The tip of a Miller-Abbott tube, which had been inserted preoperatively, presented at the opening in the duodenum. This tube was grasped, drawn into the wound for a distance of about one foot and was then passed through the distal duodenum into the jejunum to serve as a feeding tube.

As duodenal closure was started it became obvious that all carcinomatous tissue in the wall had not been excised. However, the patient's condition had become critical and more radical resection was out of the question. The duodenum was hastily closed and the line of closure was reinforced with omentum. Right hemicolectomy was completed by exteriorizing the ends of the terminal ileum and transverse colon in double barrel fashion. The oozing, infected and unperitonealized right gutter was drained through a stab wound in the right flank.

The patient improved and he left the operating table in fair condition. Postoperatively, he was given fluids, saline, and Protenum through the Miller-Abbott tube. Wangenstein drainage was established through a Levin tube in the stomach. Enteral feedings were supplemented by intravenous therapy. The ileostomy functioned well.

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On the seventh postoperative day, bile-stained fluid began to drain from the stab wound in the flank. The skin was protected with aluminum paste and suction drainage on the fistula was maintained with a Stedman pump. Except for a rising blood urea nitrogen, chemical and fluid balance was fairly well maintained until the patient developed bilateral bronchopneumonia and died on his fifteenth postoperative day. The duodenal fistula may have been a contributory, but hardly a primary cause of death.

DISCUSSION

Judging by the number of reported cases, one might conclude that duodenal fistulas are rare. We doubt that this is true. One naturally hesitates to publicize the errors in technic or mistakes in judgment made by himself or his colleagues. Undoubtedly, duodenal fistula is encountered as a complication of surgery much more frequently than our collected data would imply.

Interest in the subject of duodenal fistula was stimulated by the cases herein reported. We feel that the experience gained in the treatment of these cases has been valuable, and we present this material in the hope that it may aid others in the handling of this distressing and often serious complication.

SUMMARY

1. The cases of duodenal fistulas reported in the English literature since 1937 have been collected for review.
2. Six previously unreported cases have been added to form a small series for study.
3. The treatment of duodenal fistulas has been reviewed and commented upon in the light of our own recent experience.
4. The high incidence of spontaneous closure of the fistula on a proper supportive regimen is to be emphasized.
5. A significant decrease in mortality is demonstrated when our series is compared to the cases reported prior to 1937.

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ELECTROPHRENIC RESPIRATION

V. EFFECT ON THE CIRCULATION OF ELECTROPHRENIC RESPIRATION AND POSITIVE PRESSURE BREATHING DURING THE RESPIRATORY PARALYSIS OF HIGH SPINAL ANESTHESIA*

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THE DEPRESSION OF RESPIRATION that occasionally occurs with spinal anesthesia requires prompt and adequate treatment if the ill effects of hypoxia are to be avoided. Unfortunately, when procaine goes high enough to seriously impair respiratory activity, there occurs a fall in blood pressure and an almost complete abolition of those cardiovascular mechanisms which are capable of adequate compensation in regard to blood pressure and cardiac output. It is in this situation that the anesthetist must apply positive pressure breathing. This article will deal with the effect on the circulation of positive pressure breathing during high spinal anesthesia. An attempt will then be made to compare positive pressure breathing and electrophrenic respiration under these circumstances.

In previous publications evidence has been presented that artificial respiration can be effectively administered by applying an electrical current to the phrenic nerve and then causing the voltage of this current to be varied between 0 and a peak at that rate at which it is desired to have the animal or patient breathe.^{1-6, 18} The respiratory rate can be readily controlled by adjusting the rate of the cycling of the voltage. The tidal volume is proportional to the peak voltage applied, and thus the depth of respiration and minute volume can be likewise flexibly varied within satisfactory limits. Adequate ventilation in the experimental animal^{1, 2, 4, 5} and man^{3, 6, 18} can be obtained with the stimulation of either phrenic nerve. It has recently been found possible to produce effective electrophrenic respiration in man by applying an electrode to the skin over the cervical course of the phrenic nerve.^{6, 18}

It was further demonstrated that spontaneous respiration ceases promptly after the onset of electrophrenic respiration in both the experimental animal and man.^{1-6, 18} It became unnecessary, therefore, to be concerned with superimposing the respirator's rhythm on the patient's rhythm since the electrophrenic respirator assumes complete control of respiration. The mechanism of this prompt suppression of spontaneous respiration is reflex in nature and is mediated, at least in part, by the vagus nerves.¹⁹

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METHOD

An attempt was made to imitate conditions attending the respiratory paralysis and circulatory collapse that accompany an unexpectedly high spinal anesthesia, insofar as these could be obtained in the anesthetized animal. After Nembutal anesthesia was administered (35 mg./Kg. of body weight) a No. 6 ureteral catheter was inserted through the atlanto-occipital membrane after the method of Co Tui⁷ and was then threaded down the subarachnoid space until its tip lodged in the lumbosacral area. When it was desired to administer an "unexpectedly" high spinal block, 100 mg. of procaine hydrochloride in 5 cc. of saline were rapidly injected. This resulted in complete respiratory paralysis within four to eight minutes. Two cc. of the same solution were subsequently injected at approximately 20-minute intervals in order to maintain the animal in the desired state.

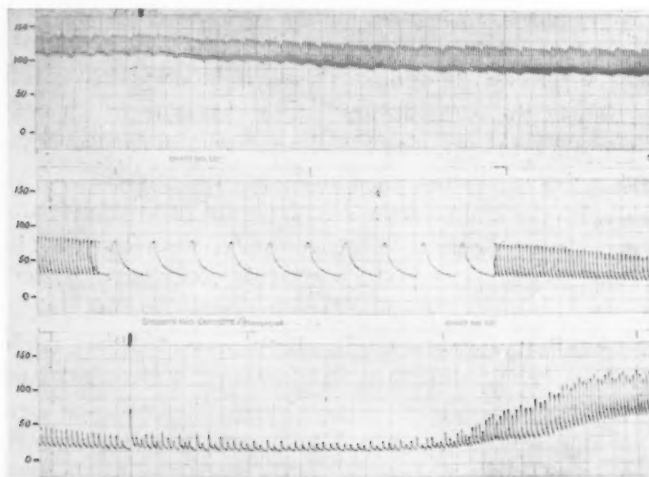


FIG. 1.—Dog under Nembutal anesthesia breathing room air. Total spinal block begun at signal in upper tracing. Electrophrenic respiration begun at signal in lower tracing. Femoral arterial pressure in millimeters of mercury at the left. Chart speed is 2.5 mm. per second except during fast tracing, when it is 25 mm. per second. Middle tracing starts 11 minutes after upper tracing. The middle and lower tracings are continuous.

Electrophrenic respiration was administered by a modified apparatus of the type previously described.* Positive pressure breathing was administered by the type of apparatus most commonly employed by the anesthetist at the time of respiratory paralysis, namely, manual compression of a rubber bag.

The breathing bag was connected to the animal's tracheal cannula by way of a soda-lime canister to provide for carbon dioxide absorption. A side arm was connected to a water manometer so that the pressure applied to the lung could be accurately regulated. The animal was made to breathe either 100 per cent oxygen or room air. Femoral arterial pressures were registered on the electromanometer* in use in this laboratory.⁸

* Courtesy of The Sanborn Co., Cambridge, Mass.

In the human subject, pneumotachograms were obtained by means of the instrument devised by Silverman⁹ and Silverman and Whittenberger.¹⁰

RESULTS

The first experiment was aimed at testing the efficacy of electrophrenic respiration in the dog subjected to respiratory paralysis and the resulting anoxia which led to clearly established cardiac insufficiency. Figure 1 is the

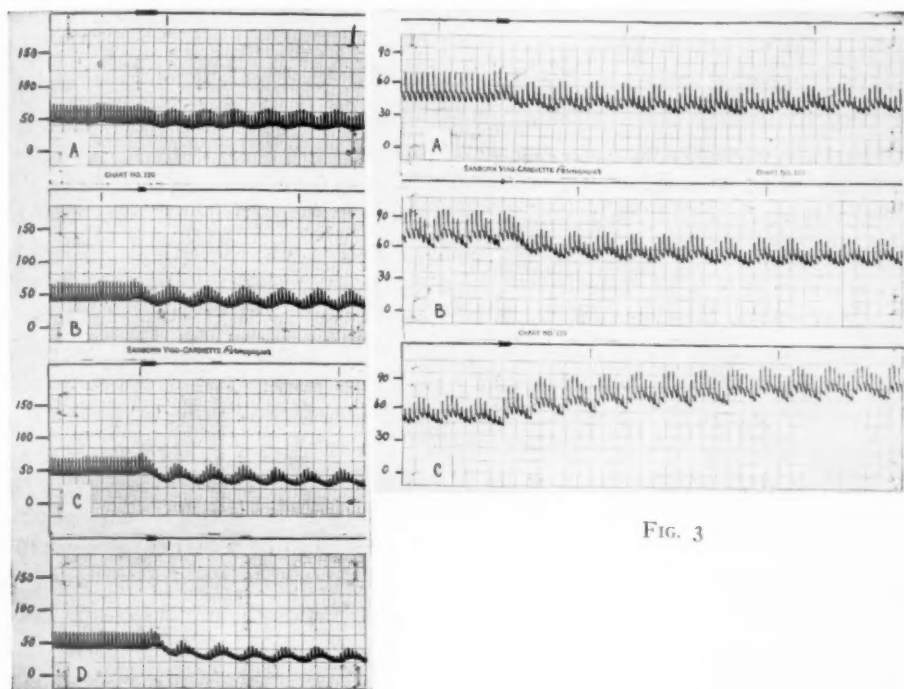


FIG. 2

FIG. 2.—Total spinal anesthesia with respiratory paralysis induced in the Nembutalized dog on 100 per cent oxygen. Intermittent positive pressure breathing with rubber bag containing 100 per cent oxygen is begun at the signal in each record. A shows the effect on the femoral arterial pressure when 5 cm. of water, intermittent positive pressure, is applied; B is the result of applying 10 cm. of water; C = 15 cm. of water; D = 20 cm. of water. Chart speed = 2.5 mm. per second. Blood pressure in millimeters of mercury at the left. These tracings were obtained within 12 minutes of each other on the same dog.

FIG. 3.—Total spinal anesthesia with respiratory paralysis induced in the Nembutalized dog on 100 per cent oxygen. The upper tracing shows the depression of femoral arterial pressure following the onset of intermittent positive pressure breathing with 15 cm. of water. The middle tracing was begun after an interval of six minutes, three minutes after the onset of electrophrenic respiration. At the signal, in the middle tracing, electrophrenic respiration was stopped and intermittent positive pressure breathing begun. The middle and lower tracings are continuous. At the signal in the lower tracing, positive pressure breathing was stopped and electrophrenic respiration was started. Blood pressure in millimeters of mercury is at the left. Chart speed = 2.5 mm. per second (See text).

tracing from such an experiment. The top tracing in Figure 1 demonstrates the fall of blood pressure following the administration of spinal anesthesia to the Nembutalized dog breathing room air. The procaine hydrochloride was injected at the signal. An interval of 11 minutes occurred between the top and middle records. The middle and lower records are continuous. At the beginning of the middle record, complete respiratory paralysis had set in and the heart was failing rapidly, as indicated by the further fall in blood pressure and the slow systolic rise seen on the fast portion of the tracing.¹¹ Electrophrenic respiration was begun at the signal on the lower tracing. The extremely low blood pressure and irregular rhythm indicate that the heart was close to the limit of its function at that time. Within 50 seconds after the onset of electrophrenic respiration, cardiac action improved and the blood pressure soon returned to 120/65 mm. Hg. The dog was then maintained in satisfactory condition for further experimentation for four hours, during which time spinal block was maintained up to and including the medulla.

In other experiments, after bringing the spinal anesthesia to the point of respiratory paralysis, endotracheal insufflation was applied at pressures of 5, 10, 15, and 20 cm. of water. Throughout these experiments an attempt was made to imitate the type of endotracheal insufflation as observed and practiced in the operating room. It can be seen from Figure 2 that the higher the pressure used during endotracheal insufflation, the more profound is the depression of the circulation. That the falls in arterial pressure observed in Figure 2 reflect similar changes in cardiac output is indicated in a later section.

Intermittent positive pressure breathing with 15 cm. water was selected for comparison with electrophrenic respiration in regard to the effect on the circulation. Figure 3 shows the results of both methods. In 3 A can be seen the effect of positive pressure breathing at 15 cm. water on the femoral arterial pressure of the dog under spinal anesthesia high enough to cause respiratory paralysis. When electrophrenic respiration was applied to the animal, the blood pressure rose (beginning of Fig. 3 B). To further contrast the effect of electrophrenic respiration and positive pressure breathing, the animal was respired by electrophrenic respiration and then abruptly switched to positive pressure respiration and vice versa. The results are shown in Figures 3 B and 3 C. The arterial pressure was at appreciably higher levels under the influence of electrophrenic respiration. Conversely, the blood pressure was depressed by changing from electrophrenic respiration to positive pressure breathing.

This type of comparison was made in eight dogs with similar results in each case. The circulatory depression produced by positive pressure breathing and the elevation of blood pressure by electrophrenic respiration was most emphatic in those animals in which the hypotension was most pronounced.

DISCUSSION

In the experiments described above it was demonstrated that in the dog suffering from the respiratory paralysis and circulatory collapse of high

FIG. 4

EFFECT OF PFB IN HEMORRHAGIC SHOCK
FEMORAL ARTERY PRESSURES

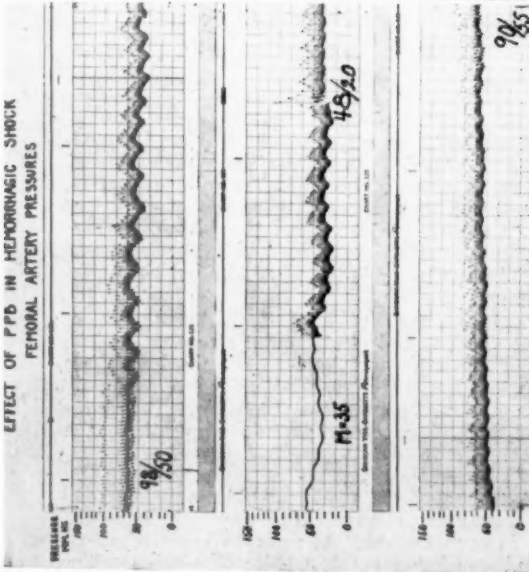
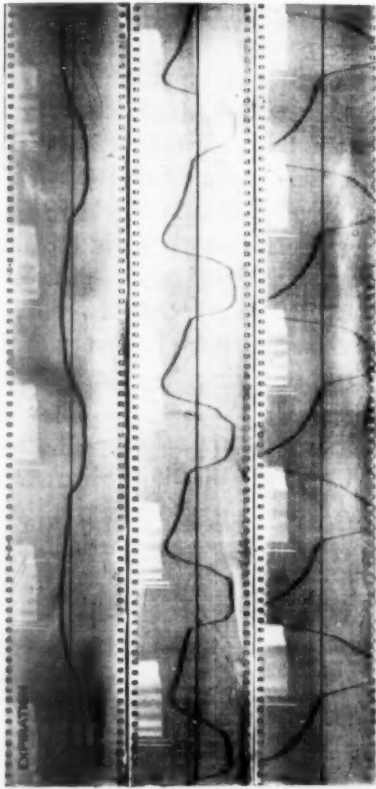


FIG. 5



A. NORMAL BLEPR C. EPR-HIGHER VOLTAGE

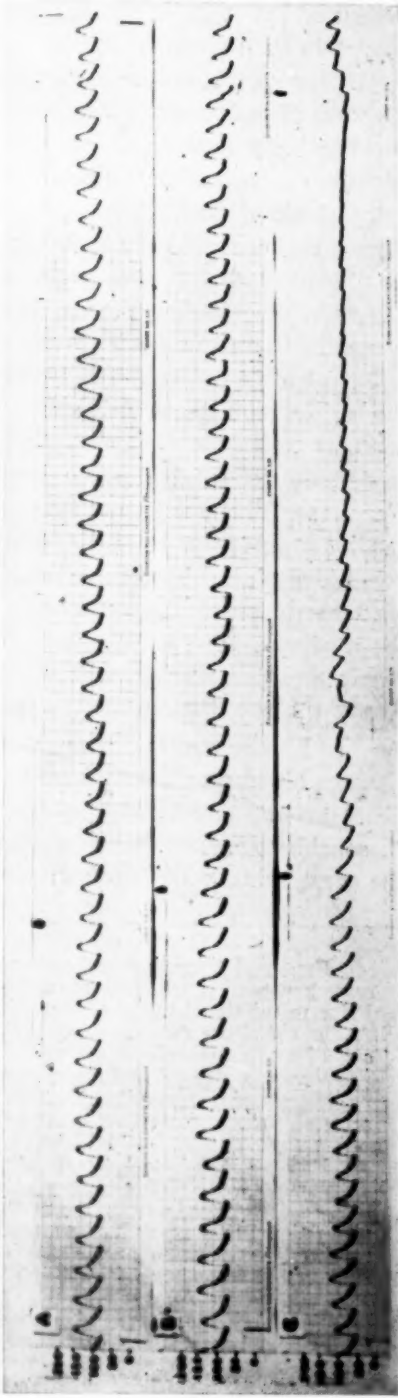


FIG. 6
(Legend on Opposite Page)

spinal anesthesia, electrophrenic respiration has a beneficial effect on the blood pressure. Intermittent positive pressure breathing, the method commonly employed in such a crisis, depresses the blood pressure.

Under spinal anesthesia, cardiac output has been found to fall and this fall becomes of major importance during high spinal anesthesia.¹² In the above-described experiments, the anesthesia was carried high enough to block the phrenic nerves and was therefore well above the uppermost portion of the sympathetic outflow. It was previously shown¹³⁻¹⁶ that sympathetic fibers are among the most susceptible to procaine hydrochloride of any in the subarachnoid space and that they are blocked appreciably before motor axones are affected. Since motor axones above the site of the uppermost portion of the sympathetic outflow were blocked in these experiments, it is certain that the animals had no unblocked sympathetic fibers traversing the subarachnoid space during the high spinal block. From this it can be assumed that the peripheral vascular resistance was relatively stable from moment to moment and therefore that a rise in blood pressure was indicative of a rise in cardiac output and vice versa. This point was made so that an indication of directional changes in cardiac output could be obtained from pressor or depressor reactions under the conditions of the above experiments.

Experiments in dogs shocked by serial hemorrhages also indicate that both the cardiac output and the blood pressure are higher during electrophrenic respiration than during positive pressure breathing.²⁰ Figure 4 is representative of the few dogs studied in this connection thus far.

The precise nature of the mechanisms by which electrophrenic respiration elevates blood pressure and cardiac output while positive pressure breathing depresses the circulation has not been critically examined. It would seem reasonable to assume, however, that positive pressure breathing retards flow in the great veins, while electrophrenic respiration has the opposite effect.

FIG. 4.—Femoral arterial pressure tracing from a Nembutalized dog with moderate hypotension following serial hemorrhages. The three tracings are continuous. Prior to the signal in the top tracing the dog was under electrophrenic respiration. At the signal the respirator was stopped and intermittent positive pressure with 15 cm. of water pressure was applied. At the signal in the middle tracing, positive pressure was stopped and electrophrenic respiration was begun. Blood pressure in millimeters of mercury is at the left. The straight line in the middle tracing represents electrically integrated mean pressure.

FIG. 5.—Pneumotachograms of spontaneous and electrophrenic respiration in a 32-year-old woman. Inspiratory volume is represented by the area above the base line, expiratory volume by the area below the base line. Tidal volume is directly proportional to the area in these tracings. A = spontaneous respiration. B = electrophrenic respiration at medium voltage. C = electrophrenic respiration at a slightly higher voltage (See Table I).

FIG. 6.—Femoral arterial pressure tracings from a 56-year-old man before and during spinal anesthesia. Positive pressure breathing applied to airway by means of anesthesia bag; started at the signal in each tracing. A, prior to onset of spinal anesthesia; B, when level of loss of pin-prick has reached D-9; C, when level of loss of pin-prick has reached D-3. Positive pressure breathing stopped at second signal. Chart speed = 25 mm. per second. Scale is in mm. Hg. at left.

The practical consideration in the evaluation of these technics is that the basic desideratum in this type of catastrophe is adequate ventilation. The authors do not agree with the contention that circulatory collapse *per se* is the cause of death in high spinal anesthesia if the horizontal or head-down position is maintained and if the circulation is not otherwise embarrassed. The presence of procaine hydrochloride around the medulla or even in the fourth ventricle has little bearing on the problem under these conditions since the efferent sympathetic pathway has already been completely blocked. Supporting evidence for this view is found first in that group of experiments in which dogs have been maintained by electrophrenic respiration for prolonged periods of time during which the entire spinal canal up to the occiput was bathed in 2 per cent procaine. In addition, it was found possible to keep a cat in good condition by means of electrophrenic respiration for 22 hours, during which time respiratory paralysis was continuously maintained by the injection of procaine into the fourth ventricle via polyethylene tubing.^{2, 17} It is felt, therefore, that if adequate ventilation is carried out without further embarrassment of the circulation, death may be averted.

In order to carry out adequate ventilation by means of positive pressure breathing, those pressures must be used which have been shown by the above data to depress the circulation under these circumstances. Further, the more one attempts to increase tidal ventilation, the higher the pressure that is required and the greater is the interference with the circulation. Also, the upper limit to which the rate of positive pressure breathing can be increased is relatively low. The contrary is true for electrophrenic respiration, since the more forcefully one makes the diaphragm contract, the greater the degree of negative intrapleural pressure and theoretically, therefore, the greater the aspiratory action of the thorax. The rate can readily be adjusted to 45 per minute if it is so desired.

From these data it would appear that electrophrenic respiration might be of some aid to the anesthetist in stimulating rather than depressing the circulation while producing artificial respiration during high spinal anesthesia. Several practical problems arise in this connection. First, one should know whether or not the contralateral lung is adequately ventilated during unilateral electrophrenic respiration. By performing differential bronchspirometry in man during spontaneous and electrophrenic respiration, it has been found that the lung on the unstimulated side does ventilate adequately by virtue of the mediastinal shift that occurs during the unilateral diaphragmatic descent.⁶ It has also been found that the arterial oxygen saturation is well maintained during electrophrenic respiration,^{3, 18} thus confirming the data which show that the lung on the unstimulated side is being well ventilated in man.

Secondly, if the method is to be of use as an emergency procedure, it is apparent that it must be capable of being rapidly applied. If it were necessary to place the stimulating electrode directly on the nerve by surgical exposure, or even probe for the nerve with a needle electrode, it would not adequately

meet the requirements of the situation. It has been found, however, that electrophrenic respiration in man is readily induced by the application of the electrical current to the skin at the motor point of the phrenic nerve in the neck.^{6, 17, 18} Figure 5 is the pneumotachogram of a 32-year-old woman to whom electrophrenic respiration was administered by external (percutaneous) stimulation. This figure and Table I demonstrate that her spontaneous tidal and minute volumes were readily exceeded by the submaximal stimulation of one phrenic nerve. This type of external electrophrenic respiration has been produced in over 500 people at the time of writing. Vagal slowing or other untoward effects have not been observed.

TABLE I.*—Comparison of Spontaneous and Submaximal, Right-Sided Electrophrenic Respiration in Regard to Tidal Volume, Minute Volume, and Flow Rate.

	Type of Respiration		
	Spontaneous	EPR-Medium Voltage	EPR-Higher Voltage
Respiratory rate per minute.....	10	20	20
Minute volume in liters.....	5.9	17.3	23.4
Tidal volume in cc.....	590	865	1,170
Average flow rate during inspiration in liters per minute.....	15.0	43.2	58.5

* See Figure 5.

The opportunity presented itself for obtaining data in one patient under high spinal anesthesia. The results are shown in Figure 6. Before the onset of spinal anesthesia, positive pressure breathing had little or no effect on the arterial pressure wave after the prompt recovery from the primary fall (A). When the loss of pin-prick was at the ninth thoracic segment, a moderate hypotensive effect followed the onset of positive pressure breathing (B). When loss of pin-prick was at the third thoracic segment, positive pressure breathing exerted a pronounced depressant effect on the arterial pressure and pulse pressure (C). The type of positive pressure breathing used here was not directly measured and may have been in excess of what is generally used. However, it is clear that when the sympathetic pathways are intact, permitting of full compensatory vascular activity, positive pressure breathing has little or no depressor effect. The same type of positive pressure breathing, applied in the presence of sympathetic blockade, depresses the circulation. Further experimental and clinical studies in support of this hypothesis will be published shortly.

CONCLUSIONS

1. Death during high spinal anesthesia is due primarily to the anoxia following respiratory paralysis rather than to primary circulatory collapse in the normal dog.
2. Further depression of the circulation is brought about by positive pressure breathing during high spinal anesthesia and is proportional to the pressures applied in the airway.

3. Adequate ventilation is the basic requirement during the respiratory paralysis of high spinal anesthesia. When this is accomplished by means of positive pressure breathing, the circulation is depressed, whereas electrophrenic respiration elevates the blood pressure and, presumably, the cardiac output.

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CARDIAC RESUSCITATION DURING OPERATIONS FOR PULMONIC STENOSIS*

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THIS REPORT DEALS with attempts at cardiac resuscitation during operations on a large group of patients with pulmonic stenosis at the Johns Hopkins Hospital. From November 29, 1944, until October 1, 1949, Dr. Alfred Blalock and his associates operated on 878 patients with a preoperative diagnosis of pulmonic stenosis. Forty-eight of these individuals form the basis of this study.

These patients manifested the usual signs and symptoms associated with pulmonic stenosis. All were cyanotic with arterial oxygen saturations ranging from 30 per cent to 85 per cent at rest. The details of surgical treatment (1) and anesthetic management (2) of these patients have been published elsewhere.

CLINICAL MATERIAL

Cardiac massage was employed in all of the patients discussed in this report. In a few instances the heart was still beating feebly or irregularly at the time massage was begun, while in most cases complete arrest, as determined by inspection, had occurred before beginning treatment.

All cases are considered together since there is no way, except by clinical judgment, of determining the necessity for cardiac massage. Even with electrocardiographic recording one may be misled by a normal tracing in a heart whose action is obviously inefficient. While admittedly inexact, the fact that massage was employed in these cases is taken as evidence that its use was necessary to maintain circulation. Some patients might possibly have survived without this maneuver, but its use by a surgeon with experience in cardiac surgery may be accepted as a reliable indication of complete or imminent cardiac arrest.

The 48 patients represent 5.5 per cent of the 878 patients operated on for pulmonic stenosis during this period. In 33 instances the surgeon was successful in restoring effective cardiac function. Of the 33 patients in whom heart beat was restored following the resuscitative attempts 18 lived for 12 hours or more. Twelve of the patients were discharged from the hospital with improvement in cyanosis and may be considered as good results. Two of these, however, had evidence of neurologic damage from anoxia. Six patients died in less than 72 hours after operation. In four of these, death was attributable to cerebral anoxia during the period of cardiac arrest. The cause of death in the remaining two patients was undetermined.

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During more than 700 operations the patient has been connected to the direct writing electrocardioscope and tracings have been taken at frequent intervals throughout the operation. This permits immediate electrocardiographic evaluation if there is any visible change in heart action or deterioration in the patient's general condition.

DISCUSSION

Cardiac emergencies under anesthesia may be divided into two main types, cardiac arrest and ventricular fibrillation. Although no instance of ventricular fibrillation has been encountered in this series, the management of this condition will be included in this discussion. Because cardiac arrest is much more frequent it will be considered first.

Cardiac Arrest. The largest group of patients with cardiac arrest has been reported by Hamilton Bailey.³ In 40 such patients he employed cardiac massage during general surgical procedures. Ruzicka and Nicholson⁴ and others⁵ have also reported cardiac resuscitation by massage. The effectiveness of this procedure in maintaining circulation has been borne out experimentally. Gunn⁶ demonstrated that a dye injected into the right ventricle of the arrested heart of a dog appeared in the lungs and carotid artery after rhythmic cardiac compression. Driggs and his co-workers⁷ maintained a systolic blood pressure of 60 to 70 mm. of mercury by cardiac massage in animals.

Thompson *et al.*⁸ found that artificial respiration would maintain measurable circulation in dead dogs which had been heparinized and injected with radioactive tracer substances. Pollock⁹ had shown experimentally that there are minor fluctuations in the blood pressure and pulse during rhythmic insufflation of the lungs. Critical analysis of these reports shows that one may expect little benefit from the circulation resulting from insufflation alone.

The subject of myocardial stimulants is controversial. Bailey was unable to initiate myocardial contractions by giving epinephrine into the heart in 40 cases of cardiac arrest. Moreover, in the presence of cardiac arrest, epinephrine may precipitate ventricular fibrillation. However, when massage has been successful in eliciting a myocardial response, epinephrine may be useful to support cardiac contractions. In ventricular fibrillation epinephrine is contraindicated because it may perpetuate the arrhythmia. Fauteux¹⁰ advocates dilute solutions of barium chloride because of the stimulating effect of the barium ion on the myocardium.

Most investigators believe that the direct myocardial action of nikethamide is negligible. The stimulating effects of nikethamide in the unanesthetized patient may be lost during anesthesia.¹¹ The studies of Eckenhoff and Hafkenschiel¹² suggest that nikethamide may be harmful to the failing heart.

The value of procaine in diminishing the irritability of the myocardium has been established. Burstein¹³ showed that procaine protects the hearts of dogs against fibrillation during cyclopropane anesthesia and that procaine may restore the heart to normal rhythm even when paroxysmal tachycardia has occurred.

From the experience with 48 instances of cardiac arrest at the Johns Hopkins Hospital certain observations are evident. The duration of cerebral anoxia is particularly significant in the cyanotic patient because the oxygen supply to the vital centers is already impaired. Whereas in normal individuals a three to five minute period of cerebral anoxia will ordinarily be tolerated, a much shorter interval of oxygen deprivation in cyanotic patients may lead to irreversible cerebral damage. We have seen severe neurologic residua after less than 60 seconds of cardiac arrest. It is apparent that resuscitative measures must be employed promptly if complete recovery is to be expected. The most important measure in resuscitation of the patient is cardiac massage. This maneuver is most effectively performed by grasping the heart in the hand and uniformly compressing or squeezing the ventricles. Frequently in children a less ideal technic of massage must be employed because of limited exposure of the heart and because the thoracic cavity may not admit the entire hand. Nevertheless one can usually place two fingers behind the heart and rhythmically compress the ventricles against the sternum. Such a method has been effective in a number of these patients. Optimal rate of massage in children is 50 to 60 times per minute.

Artificial insufflation of the lungs with a high percentage of oxygen is essential. Mechanical respirators have not been used in this clinic. While such devices offer a number of theoretical and practical advantages we have found manual compression of the anesthesia bag quite satisfactory.

Myocardial stimulants are used routinely. The dosage of drugs used in cardiac resuscitation varies widely because of the discrepancy in age and size of the patient. In the case of epinephrine the usual dose is 0.25 to 0.5 cc. of a 1 to 1000 solution. This solution is injected into the vena cava or auricles if preliminary massage has elicited a feeble response. The effect is usually favorable. If cardiac massage alone fails to produce any myocardial activity the combination of epinephrine and massage may be successful in initiating contractions.

Despite the well recognized injunctions against the use of epinephrine with cyclopropane anesthesia, we have noted no arrhythmia or fibrillary response in any of the many instances where these agents have been used together. The simultaneous use of procaine hydrochloride may account for the absence of undesirable side effects. The average dose is 8 mg. per Kg. of body weight of a 1 per cent aqueous solution of procaine hydrochloride.

Barium chloride solution (0.5 per cent) has been employed in a few patients and produced apparent increase in force and amplitude of systolic contractions. Certain other drugs cannot be recommended as resuscitative agents. Nikethamide was used regularly as a stimulant in the early group of patients with no definite beneficial effects, so that at present it is seldom employed. Caffeine sodium benzoate has been used in isolated instances without apparent benefit. Digitalis derivatives are not considered to be resuscitative medications in acute cardiac arrest. Lanatoside or digitoxin occasionally may be beneficial to sup-

port the resuscitated heart when additional strain is anticipated as the systemic-pulmonary anastomosis is opened.

Additional measures may contribute to the success of the resuscitation. The partial release or complete removal of the chest retractor is suggested as an aid to more adequate pulmonary ventilation. The Trendelenberg position favors cerebral circulation. Instruments occluding major vessels or distorting the position of the heart or great vessels should whenever possible be released. The adequate replacement of blood by transfusion or plasma infusion is obviously important.

Ventricular Fibrillation. As previously stated, no instance of ventricular fibrillation was encountered in these 48 patients with cardiac arrest. It is, therefore, assumed to be an uncommon occurrence in cyanotic patients. Nevertheless, a brief consideration of ventricular fibrillation is appropriate.

Electrical shock has been effective both experimentally¹⁴ and clinically¹⁵ in reverting fibrillating ventricles to a normal rhythm. According to Mautz¹⁶ procaine and metycaine applied topically or injected into the blood stream will defibrillate the dog's heart. By the combination of electrical counter shock with injections of procaine Beck¹⁷ was able to effect successful defibrillation in 50 consecutive dogs with experimentally produced ventricular fibrillation.

Cardiac massage is not usually recommended in connection with ventricular fibrillation. Lampson, Sheaffer, and Lincoln¹⁸ described a clinical case of acute circulatory arrest with ventricular fibrillation demonstrated electrocardiographically in which defibrillation and survival followed a combination of procaine injections and cardiac massage. The opponents of massage in ventricular fibrillation state that it will only perpetuate the rhythm by further stimulation of the hyperirritable myocardium. It is probably fair to state that massage should be less frequently and more cautiously used in cases of ventricular fibrillation than in patients with cardiac arrest. Cardiac massage must be employed to support cerebral circulation in the event that defibrillation has not been immediate.

Quinidine will prolong conduction time and increase the refractory period of the myocardium. These effects may abolish fibrillation. Physiologists have long known the effect of the potassium ion in depressing the myocardium, but this knowledge has had little clinical application because of difficulty in controlling the degree of myocardial depression.

A device (Fig. 1) has been constructed to apply electrical shock in cases of ventricular fibrillation. It utilizes a rheostat and specially constructed felt-padded electrodes (Fig. 2) to deliver a 1.0 to 1.5 ampere current from a 110 volt 60 cycle circuit through the heart. Before application to the heart, the felt surfaces of the electrodes are moistened with normal saline solution to obtain electrical contact and to prevent burning of the myocardium. Utilizing the techniques of Hooker *et al.*¹⁴ and of Beck¹⁵ with certain personal modifications the author has been successful in resuscitating dogs with electrically induced ventricular fibrillation. In these limited experimental trials the routine use of

procaine proved valuable. Supplemental cardiac massage was occasionally employed.

COMMENT

The incidence of cardiac arrest in a series of 878 patients undergoing surgery for pulmonic stenosis was 5.5 per cent. It was originally believed that with increasing experience the incidence of cardiac arrest would decrease. Now it is evident that the complication occurs largely in "poor risk" patients.



FIG. 1

FIG. 1.—Cardiac Emergency Set. The base upon which the rheostat and foot switch is mounted fits into the box when not in use. The removable tray contains the electrodes and resuscitative medications (epinephrine solution 1 to 1000, procaine hydrochloride 1 per cent solution, quinidine lactate 10 per cent solution, barium chloride 0.5 per cent solution and lanatoside solution 0.4 mg. ampules).

FIG. 2.—Padded Electrodes. The diameter of the felt surfaces is 2.5 cm. and 4.5 cm. in the two pairs.



FIG. 2

All patients with pulmonary stenosis have been accepted for operation regardless of the risk involved. In many patients it was believed unlikely that they would otherwise survive infancy. Unless such patients are denied the possible benefit of surgery this incidence of cardiac arrest will probably not be significantly reduced in the future.

Preventive measures will, of course, decrease the incidence of cardiac arrest in the poor risk patients. In Ziegler's¹⁹ study of electrocardiographic tracings

of 175 patients undergoing operation for pulmonic stenosis in this hospital it was noted that certain changes in cardiac activity precede cardiac arrest. Bradycardia of 30 to 40 beats per minute during anesthesia is the most serious of these changes. Unexplained tachycardia or extrasystoles may also serve as warnings. Prompt attention to such disturbances may prevent disaster.

Myocardial anoxia plays a major role in the etiology of cardiac arrest. The anesthetist can undoubtedly prevent many instances of arrest by constantly supplying as high a concentration of oxygen as is compatible with anesthesia. When an arrhythmia develops the depth of anesthesia is decreased and if cyclopropane is in use it is flushed out of the anesthetic system. A 100 per cent oxygen or an ether oxygen mixture is substituted. Bradycardia will often respond to complete inflation of the partially collapsed lung.

In most cases where bradycardia occurs during anesthesia atropine sulfate in a dose of 0.1 mg. per ten Kg. of body weight is injected intravenously. The heart rate will usually accelerate. Injections of the vagus nerve with procaine have not been as effective as atropine in eliminating this apparent vagal depression of the myocardium. Atropine is also a routine preoperative medication. If tachycardia or numerous extrasystoles appear, an intravenous injection of a 1 per cent procaine hydrochloride solution not exceeding 8 mg. per Kg. of body weight may elicit a favorable response. We have seen no unfavorable results from its use. In an occasional patient with known cardiac arrhythmia quinidine sulfate has been administered orally for several days in advance of operation in a daily dose of 1.0 Gm. for children and of 2.0 Gm. for adults. In these few instances, quinidine has been effective in preventing or suppressing arrhythmias during operation. Traction and torsion of the heart and great vessels should be minimized. Temporary release of the occlusive pulmonary artery may give a favorable response. If a patient does not tolerate the self-retaining retractor this may be only partially opened or hand retractors may be substituted.

If cardiac arrest occurs during anesthesia, and if resuscitation has been successful, the surgeon is faced with the question of whether or not to proceed. Important pulmonary collateral vessels may have been sacrificed in the mediastinal dissection. Thus, the arterial oxygen saturation has been further decreased in the already cyanotic patient. Without an anastomosis the prognosis for survival in the immediate postoperative period is poor. The surgeon is therefore obliged to continue with the anastomosis despite the apparent hopelessness of the situation.

SUMMARY

Cardiac massage has been required because of imminent or actual cardiac arrest during 48 of 878 operations for pulmonic stenosis.

In 33 instances it was possible to restore normal cardiac action, but only 12 of these patients survived to leave the hospital. In two of these 12 patients who were otherwise well, there were residual neurologic abnormalities as a result of cerebral ischemia during the cardiac arrest.

The management of cardiac emergencies during such operations has been discussed, and preventive measures have been outlined.

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A TECHNIC OF PORTACAVAL ANASTOMOSIS*

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ANASTOMOSIS OF THE PORTAL VEIN or one of its tributaries to the systemic venous system has become a valuable method in the treatment of portal hypertension. It is not the purpose of this paper to discuss the clinical aspects of the conditions or the indications for anastomosis. We wish only to describe a technic for side-to-side anastomosis of the portal vein to the vena cava.

The instrument used is a modification of the multi-toothed forceps used in the division of the patent ductus arteriosus¹ and for resections of coarctation of the aorta.² The blades of this clamp are broad and thin and the apposing jaws consist of rows of tiny, needlelike teeth, 40 to the inch. These teeth compress the vessel to prevent leakage and at the same time engage in the adventitia to prevent slipping without injury to the vessel wall (Fig. 1). For use in this operation the tooth-containing portion of the jaws was made 4.5 cm. long and

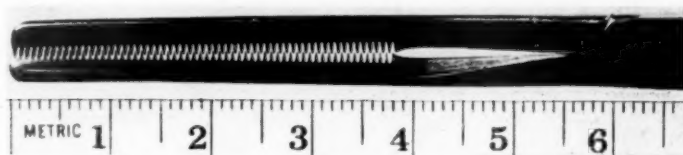


FIG. 1.—Enlarged view of forceps showing fine teeth.

the blades were curved to form a quarter arc of a circle. The handles were brought off of these curved blades at various angles to adapt the forceps to different situations (Figs. 2 and 3).

OPERATIVE PROCEDURE

Thirteen dogs, ranging from 15 to 40 pounds in weight, were operated upon under intratracheal ether anesthesia. A right thoraco-abdominal, transdiaphragmatic approach through the eighth interspace was used (Fig. 4-A) and gave excellent exposure.^{3, 4}

The portal vein was freed enough so that it could be brought over to the vena cava easily. Two 00000 Deknatel sutures were placed 2.5 cm. apart in the vein walls so that each engaged the opposing surfaces of both veins (Fig. 4-B). When these traction sutures were pulled up the veins were brought

* This study was aided by the Florence Olmstead Memorial Fellowship of the Women's Faculty Club of Northwestern University. Submitted for publication November, 1949. Instruments made by Bruno Richter, Glen Ellyn, Illinois.

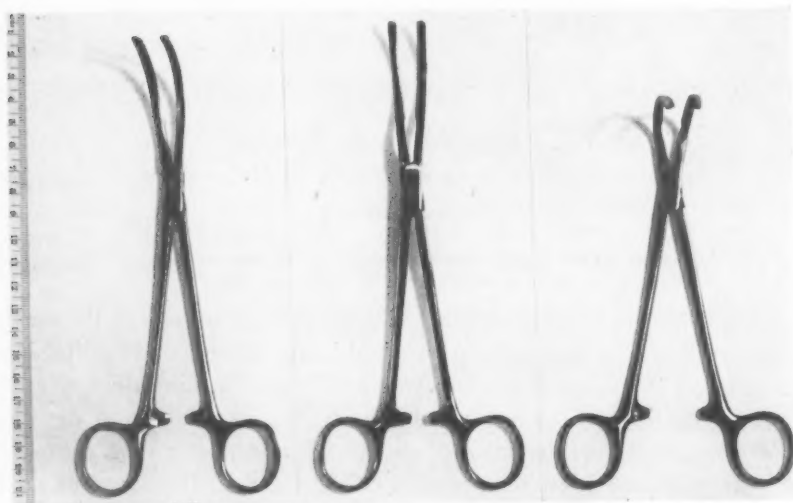


FIG. 2



FIG. 3

FIGS. 2 and 3.—Three curved, multitoothed forceps with variations in the angulation of their handles.

together and tented upward into two lips. The curved forceps were then applied with the tip caudalward. This pinches off generous lips of both vessels and holds them together for the anastomosis, at the same time allowing blood to flow through the remaining portions of the veins (Fig. 4-C).

The traction sutures were then removed and an elliptical section 2 or 3 mm. wide and, if possible, more than 20 mm. long was cut from the edge of the venacaval lip with long handled 45° angled scissors (Fig. 5-E). The lip of the portal vein was incised and slit to correspond in length and position to the venacaval opening. A side-to-side anastomosis was then accomplished using a continuous "over-and-over" suture of 00000 Deknatel silk swaged on a No. 9 curved atraumatic needle (Fig. 5-F and G). This type of suturing gave adventitia-to-adventitia approximation of the vessel edges on the posterior row of the anastomosis but allowed intima-to-intima approximation on the anterior row. After this was completed and the clamp removed there was only an

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occasional temporary ooze. The length of the completed anastomosis varied from 12 to 29 mm., depending upon the size of the dogs' veins. The diaphragm and chest wounds were closed in layers with continuous silk sutures.

RESULTS

The dogs were sacrificed at varying times postoperatively from one-half hour to four months. In all but two instances the anastomoses were widely patent (Fig. 6). In these two cases many fine strands had formed between the edges of the anastomoses, so that very little blood could flow through the openings.

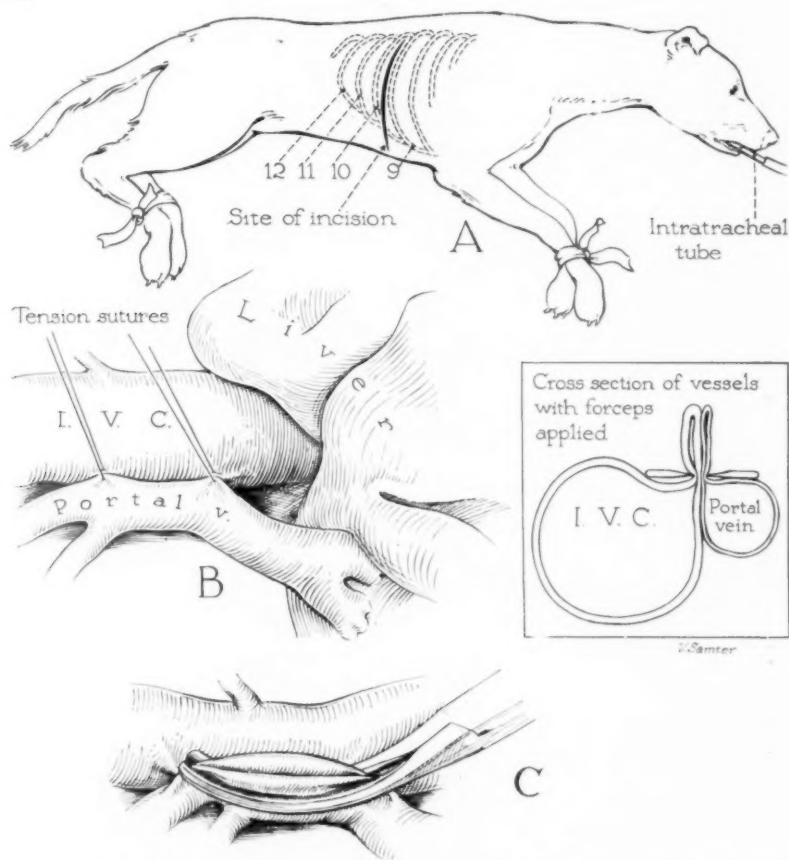


FIG. 4.—(A) Position of thoraco-abdominal incision. (B) Vena cava and portal vein with tension sutures in place. (C) Two vessels with curved forceps applied (insert shows cross section of this).

In four dogs the portal veins were ligated proximal to the anastomosis. On a regular diet these dogs became emaciated, but there seemed to be no tendency toward wider patency in their anastomoses as compared with those without ligation of the portal vein.

There was a tendency for a small web to fill in the caudal angle of the anastomoses in five instances. In five dogs the vessel edges on the posterior row of the anastomoses were everted, giving an intima-to-intima approxima-

tion around the entire anastomosis. This was somewhat difficult to accomplish and did not seem to alter the final size of the anastomosis or the web formation. Microscopic sections showed that there was rapid healing together of the vein edges with minimal reaction at the suture line (Fig. 7).

Different methods of making the openings in the two veins were tried. Longitudinal slits in both veins did not seem to give a wide enough anastomotic opening (Fig. 8-A). Excising elliptical portions of both veins tended to occlude the portal vein. This was fatal in dog 2, since the veins were so small that the

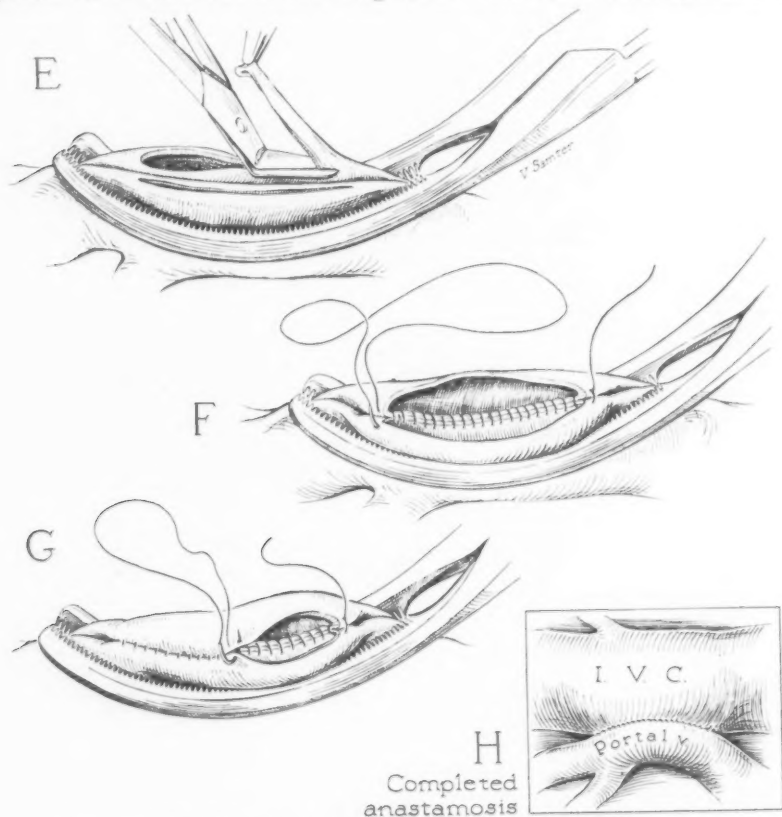


FIG. 5.—(E) Ellipse being excised from vena cava. Incision in portal vein is also shown. (F) Posterior suture row of anastomosis has been completed. (G) Anterior suture row is being sewn (the vessel edges are actually slightly everted on this row). (H) Completed anastomosis.

distended width of anastomosis became as great as the remaining circumference of the portal vein (Fig. 8-B). It was found that excision of an elliptical section of the vena cava and a longitudinal slit in the portal vein gave the best appearing anastomosis (Fig. 8-C).

The results are summarized in Table I.

COMMENTS

Partial occlusion of a vessel during anastomosis is not new.^{5, 6, 7} However, the technic described above is greatly simplified by the use of the curved-jawed,

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TABLE I.

Exp. No.	Size of Anastomosis	Eversion of Posterior Row	Ligation of Portal Vein	Duration of Anastomosis	Appearance of Anastomosis
1	12 mm.	0	0	9 weeks	Open
2	18 mm.	0	0	½ hour	Open (see text)
3	22 mm.	0	0	3 weeks	Open
4	22 mm.	0	0	17 weeks	Open
5	22 mm.	0	Yes	9 weeks	Open—web at lower angle
6	24 mm.	0	Yes	8 days	Open—web at lower angle
7	15 mm.	0	Yes	10 weeks	Open
8	22 mm.	Yes	0	17 weeks	Open
9	22 mm.	Yes	Yes	4 weeks	Open—web at lower angle
10	29 mm.	Yes	0	6 weeks	Open—web at lower angle
11	16 mm.	Yes	0	15 weeks	Almost closed
12	24 mm.	Yes	0	5 weeks	Open—web at lower angle
13	24 mm.	0	0	10 weeks	Almost closed

FIG. 6



FIG. 7

FIG. 6.—Postmortem specimen of a patent anastomosis, experiment 4.

FIG. 7.—Microscopic section through the suture line showing firm healing with minimal reaction.

multi-toothed forceps. These forceps are easy to apply with minimal dissection, and there is very little apparatus to manipulate or obstruct the field. It is practically impossible for them to slip off the vessels.

These forceps caused no injury to the vessels. Immediately after the forceps were removed at operation a row of fine dots could be seen where the teeth engaged in the adventitia, but these disappeared rapidly.

At autopsy, superficial, fine, white lines could be seen where the forceps had been applied, but microscopic sections revealed no disruption of the vessel walls in those areas.

All of the various types of multi-toothed forceps must be machined delicately for the type of work they are to do. Forceps used for coarctation of the aorta are medium in length, made of heavy stock and designed to grasp and

occlude a thick-walled vessel. There must be little or no interdigitation of their teeth, otherwise the vessel wall might be crushed and fragmented. The curved forceps used in this procedure, on the other hand, have a good deal of "spring" at their tips because of their length and curvature. They are designed to be used on thin-walled vessels. Because of these two facts, there must be a moderate degree of interdigitation of the teeth at the tip of the forceps, as shown in Figure 1, in order to prevent leakage of blood.

These curved forceps have been used to partially occlude the pulmonary artery during a subclavian-pulmonary anastomosis when complete occlusion of the pulmonary artery would have caused asphyxiation.⁸ They can also be used to advantage in doing an end-to-side

splenorenal shunt.* Lacerations of the pulmonary artery and large veins can be controlled quickly and repaired by application of these forceps.

The same principle of partial occlusion and coaptation of lips of two vessels has been used in attempting to benefit two patients with transposition of the great vessels. The curved, multi-toothed forceps were applied to the aorta and pulmonary artery near to their origin, and a large side-to-side anastomosis was made with relative ease. Although theoretically this should give better

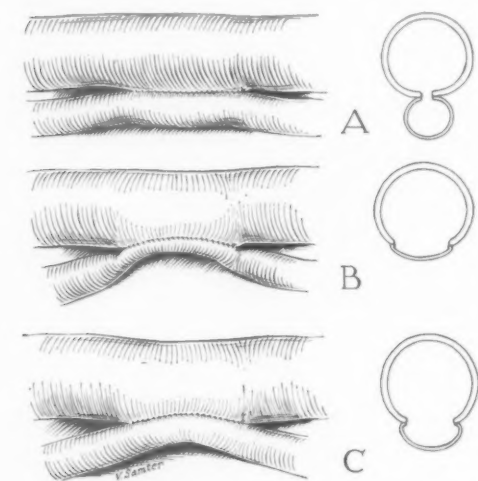


FIG. 8.—Results of various technics of side-to-side anastomosis. (A) Longitudinal view and cross section through center of the anastomosis when each vessel was slit. (B) Longitudinal view and cross section of anastomosis when elliptical portions were excised from both veins. (C) Longitudinal view and cross section of anastomosis when an elliptical portion was excised from the larger vein and the smaller vein was incised.

* Since the submission of this article the forceps have been used to good advantage in end-to-side splenorenal shunt on a ten-year-old boy with Banti's syndrome and rather severe portal hypertension.

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mixing of the two circulations and improve the condition, both patients died postoperatively of heart failure.*

CONCLUSIONS

1. A technic of side-to-side portacaval anastomosis is described that gave good results in experimental surgery.
2. The ease of this technic was made possible by the use of a new type of forceps, which is described.
3. These forceps have been used in other procedures.

* This technic has been used to accomplish aortic-pulmonary anastomosis on a ten-day-old child with tricuspid atresia whose aorta was so small that the usual Potts-Smith clamp could not be applied.

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NOTICE

The 1950 Convention of The Association of Military Surgeons of the United States will be held from November 9 to November 11, inclusive, at the Hotel Statler, New York City. The programs will deal with Civil Defense, the Defense Role of the Physician, Aviation Medicine, Rehabilitation, Military Medicine, Surgery, Sanitation, and discussion on the use of the newest therapeutic and prophylactic agents in emergency conditions.

The Convention has been organized to provide Section meetings for Dental, Nursing, Veterinary, and other specialty groups. Several of the sessions will be directed to the problems of the Medical Reserve.

TRANSLUMBAR AORTIC PUNCTURE AND RETROGRADE CATHETERIZATION OF THE AORTA IN AORTOGRAPHY AND RENAL ARTERIOGRAPHY*

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SINCE DOS SANTOS¹ INTRODUCTION of translumbar needle puncture of the aorta for abdominal arteriography 20 years ago, there have been numerous favorable reports on the subject.²⁻¹⁰ The chief criticism of the method and its dangers, based on an experimental study in dogs, is found in the work of Henline and Moore.¹¹ Time and the experience of many investigators have answered or overcome most of these objections. Arteriography is accepted as a valuable adjunct to diagnosis in demonstration of cerebral and cardiac pathologic conditions.^{12,13} Although aortography has lagged a little behind these fields in general acceptance, it seems certain that it is a useful and safe addition to other diagnostic methods in special cases of renal disease and of vascular disease of the aorta and its branches.

The chief purpose of this paper is to describe a method of retrograde catheterization of the aorta through one of the branches of the femoral artery for the purpose of injecting radiopaque media at any level desired to outline the branches of the aorta. In addition, we wish to comment on a few minor differences in technic in our use of the translumbar needle method.

NEEDLE PUNCTURE OF THE AORTA

In the past two years our experiences with needle puncture of the aorta and injection of radiopaque media have paralleled those reported by others. In general the technic of Dos Santos so well described by Nelson^{3,4} and by Wagner⁸ has been employed.

Technic. Figures 1 and 2 demonstrate the regional anatomy as the patient lies face downward. There are a few minor changes in the technics already described:

The patients have always been anesthetized, usually with Pentothal but occasionally with spinal anesthesia. In children we have used Vinethene and ether.

Needles larger in diameter than those recommended by others have been used. Two long (15 cm.) spinal needles, No. 16 and No. 17, were specially constructed for this purpose. The six inch length is essential in adults. After early experiences with No. 19 and No. 20 needles it became apparent that

* This work was possible through the unfailing co-operation of Dr. Robert D. Sloan of the Department of Radiology. Submitted for publication September, 1949.

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larger caliber needles were not dangerous and also afforded a more rapid injection of the roentgen ray opaque medium, which is essential to good visualization of the vascular pattern.

The roentgen ray examination is conducted on an ordinary radiographic table containing a Buckey grid and an overhead 200 MA tube, with the patient in prone position. An exposure time of $1/15$ second is used to prevent blurring due to motion. Other factors include a 36-inch tube-film distance, a kilovoltage ranging from 80 to 95 and 13 MAS.

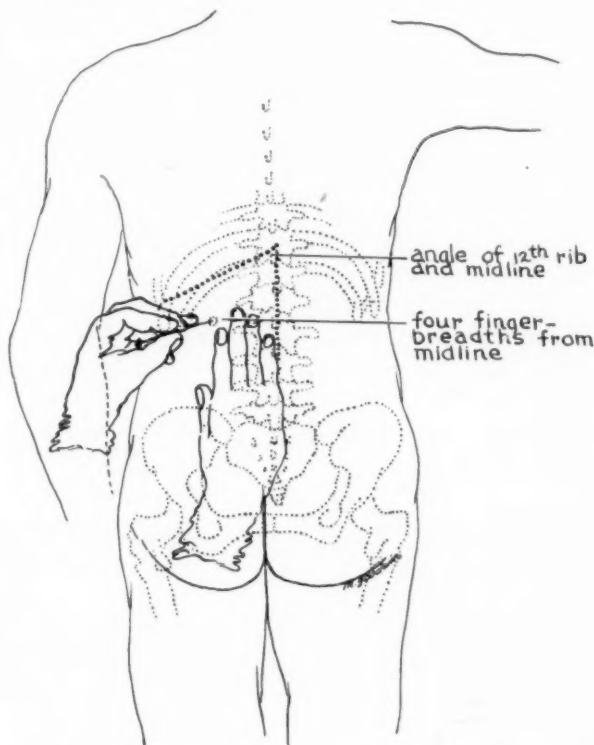


FIG. 1.—Site of needle injection for translumbar aortography. Patient is prone.

Four different contrast media have been tried: 80 per cent sodium iodide, 70 per cent "Diodrast," "Thorotrast," and 75 per cent "Neo-iopax." They all seem to offer about equal results. Usually "Neo-iopax" is used. Injections up to three times the usual dose for intravenous pyelography have been given in one afternoon. A "test dose" has been employed after a fashion, in that all the patients have had excretory urograms at least 24 hours prior to arteriography.

We have not used a pressure pump as recommended by others. All injections have been by hand syringe.

Patients under spinal anesthesia have noted a brief wave of "heat" and a short period of dyspnea as the dye returns through the cardiorespiratory sys-

tem. There is usually a slight transient blood pressure drop following injection. In two cases, where the dye extravasated during injection under spinal anesthesia (Fig. 3a), the patients complained of extreme pain for five to ten minutes. This rapidly subsided, however, and a subsequent film (Fig. 3b) showed complete absorption of the dye. There were no apparent lasting ill effects from this mishap.

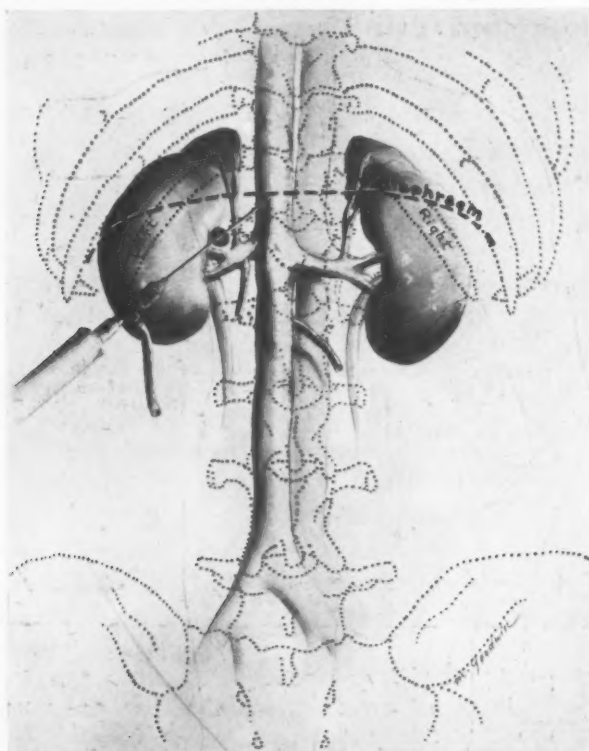
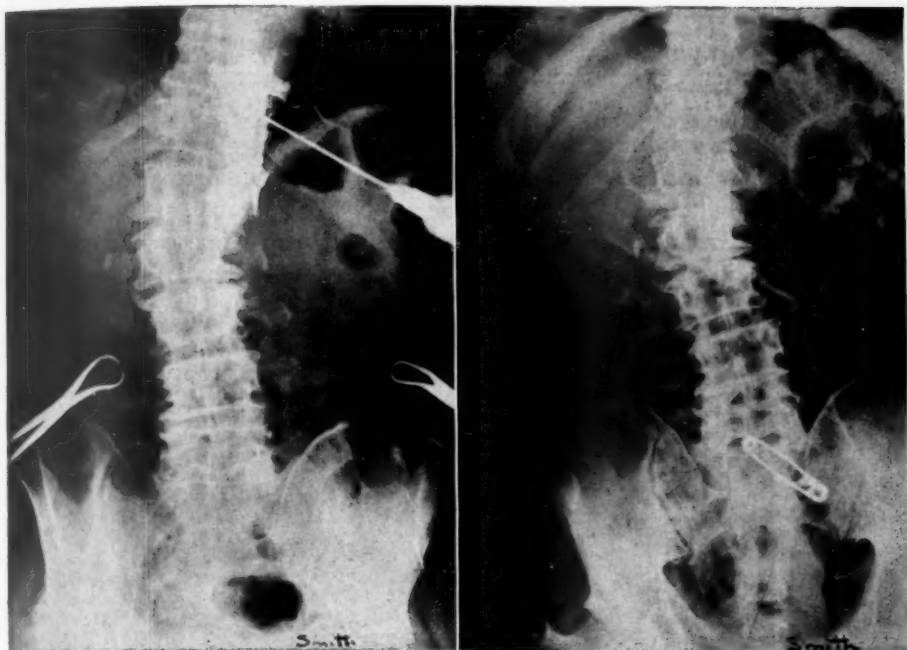


FIG. 2.—Approximate area of aorta which is neededled.

In order to prevent extravasation of the dye due to inadvertent movement of the needle after a satisfactory aortic tap has been made, it is useful to place a supporting hemostat on the needle close to the skin. This prevents movement at the time of injection.

In one case, (Fig. 4), the needle method was used to demonstrate pathologic changes in the left iliac artery. The aortic puncture was made in the usual fashion at L-1, after attempts at the levels of L-3 and 4 failed. A tourniquet was placed on the right thigh so that all the dye would go down the left side where an arterio-venous aneurysm was suspected because of swelling and pulsation in the left leg. The injection of "Neo-iopax" was made in three seconds, as usual, and the taking of the roentgenogram in the pelvic area was delayed for one second after the end of injection. The roentgen rays revealed multiple arteriovenous anastomoses. Exploration of this lesion by Drs. Alan Woods, Jr., I. Ridgeway Trimble, and C. R. Hanlon confirmed this.

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A

B

FIG. 3.—(A) Extra-aortic extravasation of dye in needle aortograph. (B) Follow-up film on same patient 24 hours later. No ill effects observed.



FIG. 4.—Multiple arteriovenous anastomoses in left iliac region.

In another case (Fig. 5) this same technic was used to demonstrate the circulation to a calcified pelvic aneurysm of the right hypogastric artery. The patient was later explored and the vessels to the aneurysm ligated by Dr. William Grose,¹⁴ who will report the case in detail. He states that the aortogram was like a map of the area involved.

The needle puncture method has been used in five children with two failures due to inability to needle the small aorta. There were no ill effects observed although extravasation of the dye occurred in two of these cases. Figure 6 shows the findings in an 18-month-old child, a patient of Dr. Lawson Wilkins

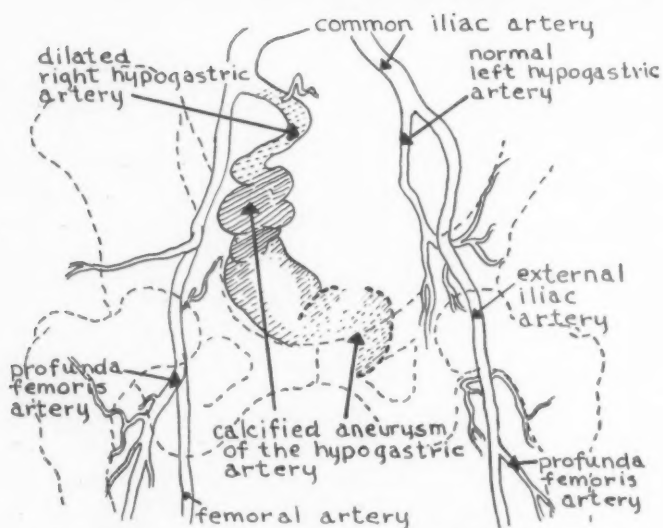


FIG. 5.—(A and B) Aneurysm of right hypogastric artery. Note also the delineation of the minor branches of the profunda femoris. Compare with Figure 8.

TRANSLUMBAR AORTIC PUNCTURE

and Dr. Hugh Jewett, with adrenal cortical hyperplasia who was suspected preoperatively of having an adrenal tumor. The left adrenal area (from which at operation a 25 Gm. hyperplastic adrenal was removed) is not outlined, for reasons unknown to us. The region above the right kidney shows a dense area of concentration of the dye, which corresponded to the hyperplastic adrenal seen on that side at exploration. Figure 7b shows a needle aortogram and left retrograde pyelogram in an 11-year-old boy with a hypoplastic, non-functioning left kidney and a large hydronephrotic right kidney. (Compare with 7a, the intravenous pyelogram in the same patient.) He also had progressive hyper-

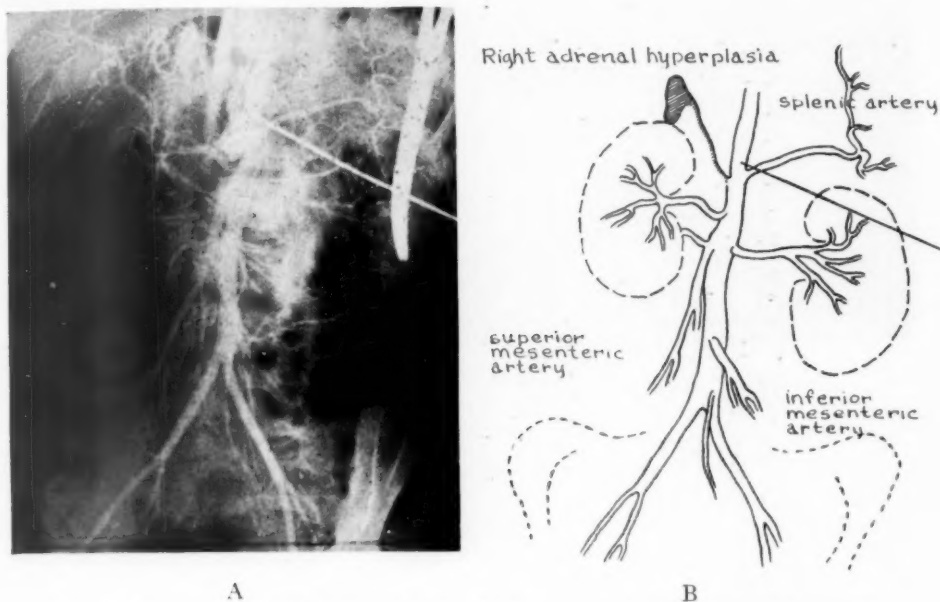
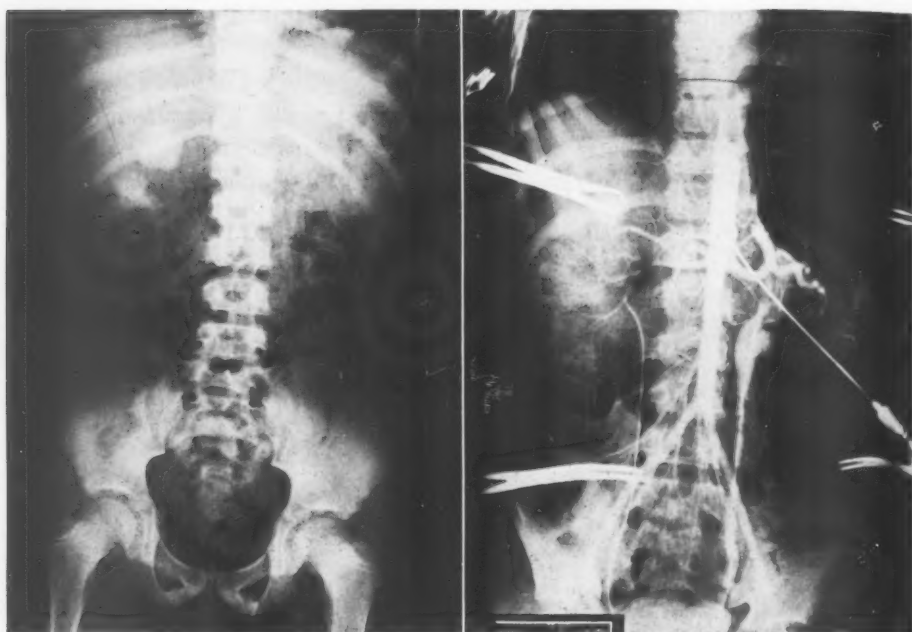


FIG. 6. (A and B) Cortical hyperplasia of right adrenal demonstrated by needle aortography. The equally hyperplastic left adrenal is not seen.

tension. Unfortunately, he died after an attempt to remove the obstructing stone from the right kidney. The autopsy findings confirmed the aortographic picture in every detail. The site of the needle puncture could not be found. We are not aware that aortograms have heretofore been made on such small children. However, except for the fact that a smaller (No. 19 or No. 20) spinal needle and less dye (five to ten cc.) were used, there is no difference in the technic.

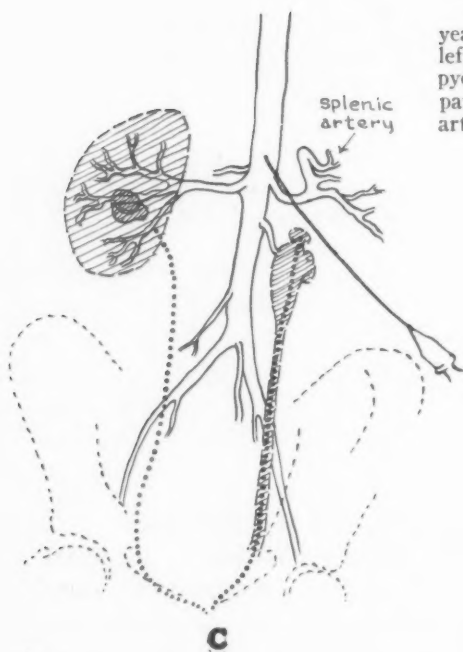
RETROGRADE CATHETERIZATION OF THE AORTA

In 1941 Farinas¹⁵ described retrograde catheterization of the aorta for making aortograms. His method, which he has reported frequently since,¹⁶⁻¹⁸ involves exposure of the femoral artery under local anesthesia and introduction of a catheter through a trocar inserted directly into it. The catheter is moved to the desired level near the renal arteries, and injection of the radiopaque medium is carried out. Afterward the opening in the femoral artery is closed



A

B



C

FIG. 7.—(A) Intravenous urogram of 11-year-old boy with right hydronephrosis and left renal hypoplasia. (B) Combined left pyelogram and needle aortogram in the same patient. Note extremely small left renal artery. (C) Diagrammatic representation.

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with arterial silk. He claims good results and no complications. So far as we know, however, no one else has reported on the use of his method.

We were aware of his work when, in 1947 and 1948, we were interested, for another purpose, in demonstrating radiographically the renal circulation in dogs.¹⁹ In early experiments the trocar method was tried but it was soon apparent that the relatively small caliber of the femoral artery in the dog did not allow insertion of a sufficiently large trocar and catheter to secure good aorto-

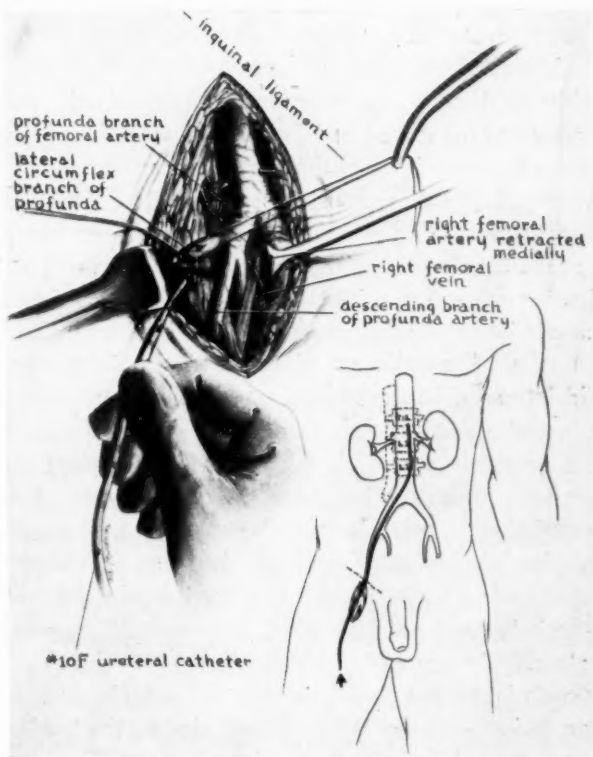


FIG. 8.—Method and site of retrograde catheterization of the branches of the femoral artery in the catheter method of aortography. Compare with Figure 5.

grams without destroying the artery. This was not serious in acute animal experiments, but because of the unfavorable experience we have never dared to try it in human beings. As the work progressed, we learned in animals to pass ureteral catheters after direct exposure and cannulation either up the femoral arteries or downward from the left carotid or the left brachial arteries. The obvious advantage of this method is that the column of injected roentgen radiopaque material may be placed in high concentration at any level desired.

We wondered whether this method might not be applicable to human beings. A femoral dissection made in three cadavers revealed a fairly constant representation of the lesser branches of the profunda femoris commonly

described in anatomy texts and recorded here in Figure 8. It seemed reasonable to assume that one of these branches might be used for the purpose of passing a large ureteral catheter upward into the aorta and that permanent interruption of the relatively minor circulation of such a vessel would not be harmful. Accordingly, this has been tried in a small series of patients.

The Method. A preliminary intravenous urogram is carried out on some day prior to the aortogram. On the day of the procedure the patient is prepared for anesthesia, and exposure of the femoral artery and its branches and insertion of the catheter is carried out in the operating room. Pentothal anesthesia has been used chiefly, although spinal anesthesia has been used occasionally. It could probably be done easily under local anesthesia, if desired. Figure 8 shows the anatomy and the site of incision. Usually the right leg is used because it is more convenient to work from that side in our roentgen ray room. However, in one case the left side was used when a second procedure was carried out on the same patient. The dissection is not difficult, but it can be very tedious. The profunda femoris frequently lies high in the thigh, and its small circumflex branches run quite laterally and deeply. After the lateral circumflex branch of the profunda femoris is identified and dissected free, two traction sutures of medium silk are placed under it. The more distal one is ligated and held laterally. The proximal one is placed on sufficient tension to control bleeding, and a small nick is made with scissors in the artery between them. Then the ureteral catheter is introduced and passed upward 35 cm., which is the usual approximate distance to the renal arteries. It is important to use as large a catheter as possible in order to secure maximal concentration of the injected dye. A No. 10 F catheter is very satisfactory. Before the catheter is introduced, a large needle is placed in the proximal end and a three-way stopcock is fixed on the end of the needle. The catheter is washed with saline to clear its lumen and to leave it full of a column of fluid, and the three-way stopcock is turned "off" so that the arterial blood will not flow into the catheter. It is sometimes very difficult, due to the angle of the vessels, to get the catheter started into the femoral artery. At this point, the assistant can often guide the tip of the catheter by pressure with his fingers outside the vessels. Once into the femoral artery, the catheter is easily passed upward to any height desired. It is then tied securely in place with the more proximal traction suture; and after suitable covering with sterile drapes, the patient is transferred to the roentgen ray rooms where the aortograms are made. It is very important to keep the catheter from being plugged with clots from the time it is introduced until the end of the procedure. To this end, an infusion of saline is attached to the three-way stopcock, and one of the team almost constantly injects small amounts of fluid. The arterial pressure is normally too high to allow for easy gravity flow. At first a mixture of saline and heparin was employed, but this is not necessary as long as the catheter is frequently irrigated. In the course of such a procedure a patient may receive as much as 1500 cc. of saline in an hour or an hour and a half. The roentgen ray technics are the same as those described in the needle method. A scout film is first

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taken, and at this time a pilot injection of four to five cc. of "Neo-iopax" is made. When the film is developed, the exact position of the catheter in relation to the renal or other desired arteries is determined; and the catheter is adjusted either up or down in order to get the optimum result with later films. Then two or more aortograms are made. In the first, 30 cc. of "Neo-iopax" is injected as rapidly as possible from a "Luer lock" syringe. The roentgen ray exposure is made at the end of injection. This film is seen before the last aortogram is made. If indicated, the catheter is still further adjusted. Next another scout film is made, as an excretory pyelogram is often present by this time. Then the last exposure is carried out at the end of rapid injection of 10 to 12 cc. of the contrast medium from a small "Luer lock" syringe. Finally, the catheter is slowly removed after further infusion of saline. The suture holding the catheter in the artery is cut and another traction suture is placed. As the catheter is removed, the artery is held under tension and securely tied. The wound is then closed with interrupted black silk sutures.

Results. The femoral artery catheterization has been carried out 15 times in 14 patients. One patient had the procedure done twice, first on the right side and then on the left where the circulation, though not exactly the same, was comparable and satisfactory for the purpose. The results with the exceptions noted below under "Complications," were all very satisfactory.

In only two cases, however, was information gained that would not have been learned from the translumbar needle puncture method. These are shown in Figures 9 through 11. The patient represented in Figure 9 had coarctation of the thoracic aorta with an aneurysm below the coarctation. His case is fully reported by Dr. Caroline Thomas.²⁰ As seen in the roentgenogram, the aortic catheter was passed its full length upward until it coiled in the aneurysm. Simultaneously another catheter was passed downward from above through the radial artery by Dr. Harry Muller, using the method described by Radner²¹ and Broden.²² These catheters were then injected separately and together in order to demonstrate the circulation.

Figure 10 is an unusually clear demonstration of the renal circulation in an 80-year-old man with arteriosclerosis. Filling defects in the renal arteries, which we have identified as arteriosclerotic plaques as described by Blackman,²³ are readily identified. Figure 11 is a pelvic arteriogram of the same patient, demonstrating the generalized arteriosclerosis.

Figure 12 shows clearly the result of this method in our first case (B.U.I. No. 38460, October 9, 1948), a patient with a normal right kidney who had had a left nephrectomy for hypernephroma. There is a recurrence of the tumor occupying the left flank area, and the stump of the left renal artery is seen coursing upward to the left adrenal area. The hazy filling of many small vessels in the tumor is typical. These findings were confirmed at autopsy later when the patient died of the tumor. There were no demonstrable ill effects from the catheter aortography.

Complications. There have been no serious complications or reactions. However, there have been several troublesome mishaps, which may be attributable



FIG. 9A



FIG. 10A

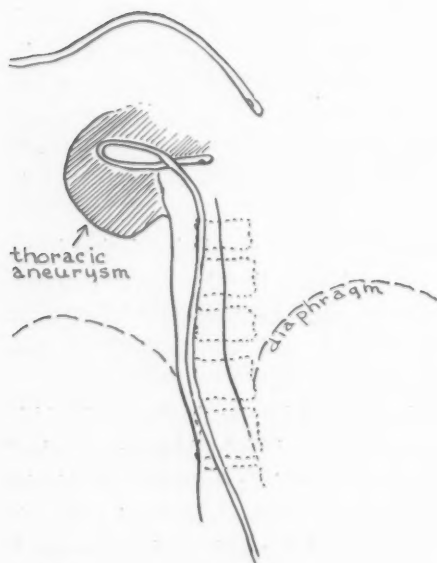


FIG. 9B

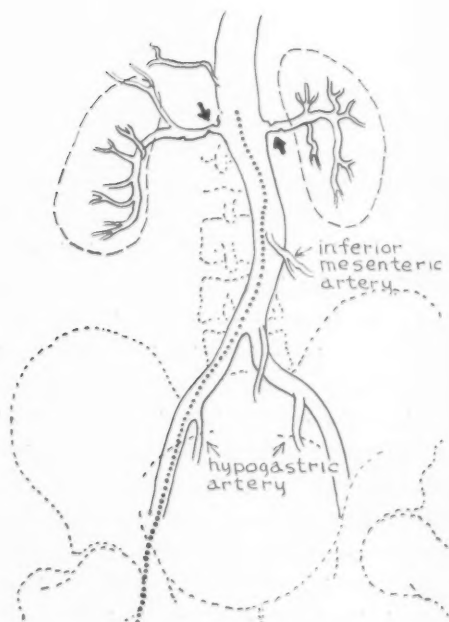


FIG. 10B

FIG. 9.—(A and B) Catheter method of aortography in patient with large aneurysm of thoracic aorta.

FIG. 10.—(A and B) Catheter method showing arteriosclerotic nicking of renal arteries. Note absence of filling of the coeliac axis due to correct position of the aortic catheter.

TRANSLUMBAR AORTIC PUNCTURE

to the method but which are more likely related to the fact that it was a new technic. In one case, early in the series, the procedure was attempted but was abandoned when the profunda femoris could not be identified. In another case, after satisfactory introduction of the catheter, it could not be passed beyond the iliac bifurcation, presumably due to arteriosclerosis. The catheter was not forced. The most serious complication occurred during an attempt to pass a catheter through the nearly obliterated femoral vessel of a one-legged man with thromboangiitis obliterans. Obstruction was met in the region of the iliac vessels. Ill-advised force was used and subsequent films showed that the catheter had passed out of the artery into the perivesical region. After considerable thought and consultation, the catheter was removed and the patient was watched carefully. No apparent ill effect was noted. It probably would not have been possible to remove the catheter without mishap had not the artery been almost obliterated by the patient's disease. One patient developed a troublesome inguinal adenitis after the procedure, and in another there was a minor wound breakdown because of delayed healing. One or two patients have complained of a temporary numbness over the thigh when the lateral femoral cutaneous nerve was inadvertently traumatized. In two cases we have had moderately severe hemorrhage at the time of catheterization because of difficulty in starting the insertion of the catheter. This was readily controlled with traction sutures, however, and the catheter was then passed relatively easily after an assistant helped to guide it through the sharp angle leading into the femoral artery. One patient, a farmer, complained of residual weakness of flexion of the right thigh, presumably due to interference of the blood supply to the right thigh muscles. When last seen, two months after the procedure, he had noted improvement, but stated that he still had some difficulty in acute flexion of his leg, as for example in climbing fences. None of this small series, or of the larger series of needle aortograms have suffered iodism or any recognized change in renal function. There have been no other recognized complications. The retrograde catheterization method has often been tedious and time consuming.

DISCUSSION

Aortography, both by the translumbar needle method and by the method of retrograde catheterization of the aorta has in our experience been a safe and often useful procedure. We do not believe that it will ever become a routine diagnostic procedure, such as pyelography. However, there seems to be no good reason why it should not be used in all cases of imperfectly visualized kidneys and of renal masses of doubtful nature. It has unquestionably great use in vascular lesions involving the aorta and its branches.

We agree with Wesson⁵ in his evaluation of the procedure, "... (the) method well fulfills the four rules of perfect diagnosis: viz., (1) a guide to treatment, (2) answers the question of prognosis, (3) satisfies the curiosity of the doctor, and (4) is without hazard in his hands."

The greatest need, as emphasized by others,⁶ is for greater experience in the interpretation of the angiograms. To this end aortography should be more



FIG. 11A



FIG. 12A



FIG. 11B

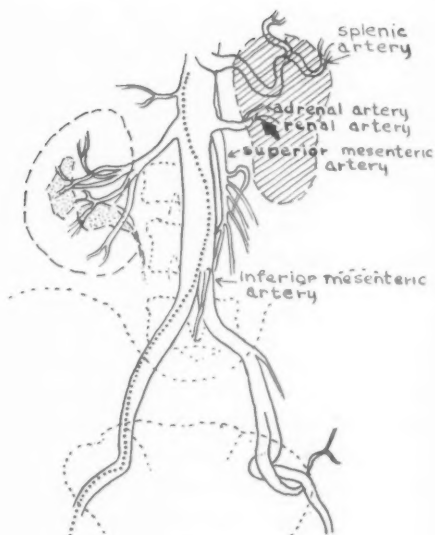


FIG. 12B

FIG. 11.—(A and B) Pelvic angiogram of the same patient as Figure 10.
FIG. 12.—(A and B) Combined excretion urogram and catheter aortogram in patient with recurrence of tumor after left nephrectomy for hypernephroma.

often employed, as we are now frequently in the position of securing rather good angiograms without being able adequately to interpret them.

The obvious advantage of being able to place the catheter at any level has not been fully exploited. It is possible, for instance, to get excellent renal detail without filling all of the coeliac axis (Fig. 10), a matter that is left only to chance in the needle puncture method. It should, theoretically, be possible to get good segmental filling at almost any level of the aorta—a factor that might be useful in the study of aortic aneurysms and of adrenal tumors. Farinas has described the use of this method in attempting to give concentrated medication to a given area. This might also be considered here too—as for instance in giving a large chemotherapeutic dose directly to the kidneys in pyelonephritis. The method might also have application in the administration of radioactive isotopes to a given locale.*

It is of interest to compare the translumbar needle method and the retrograde catheterization method. Both methods seem safe, and each gives satisfactory visualization of the renal and other vessels under optimum conditions. The chief advantage in the catheter method lies in the possibility of placing the dye injection at any level. The needle method is, however, much simpler and quicker after facility is gained in the technic of aortic tap, and the complications are fewer. This more than outweighs the advantage of the catheter method in our experience. At present we believe that the needle method of aortography is the procedure of choice. If that fails or is unsatisfactory for any reason, the catheter method should be employed.

On the other hand, in cases of aneurysms of the aorta or its branches, the catheter method might be preferred. Likewise, in the hands of the occasional operator who desires the information available from abdominal or thoracic arteriography for a special case but who has not had the time or the occasion to school himself in the needle method, the catheter method may be most suitable. It can, however, be very trying, and the procedure should not be undertaken lightly.

The reports from Sweden^{21,22} of the use of the catheter method for thoracic aortography after the catheter has been passed through the radial artery are of great interest. They have necessarily used smaller catheters than described here, due to the small size of the vessel, and one wonders whether they might not obtain better filling of the aorta with larger catheters. It also seems that the use of one of the main arteries of the arm is potentially more hazardous than the use of a small branching vessel in the leg. It may be that the femoral artery catheterization method would be as well or better suited for thoracic angiography.

SUMMARY

The subject of abdominal aortography and arteriography is discussed and briefly reviewed.

* Following submittal of this manuscript for publication, an excellent report of the use of this principle was brought to our attention. See Bierman, H. R., E. R. Miller, R. L. Byron, K. Dod, D. Black and K. Kelly: Intra-Arterial Catheterization in Man. *The Bulletin of the University of California Medical Center*, 1: 84, 1949.

Some experiences and minor differences in technic with the accepted translumbar needle method of aortography are described.

Another method of thoracic and lumbar aortography and arteriography is described. It involves the retrograde passage of a ureteral catheter through the lateral circumflex branch of the profunda femoris and into the femoral artery to the aorta. Some experiences with this method in 15 procedures on 14 patients are recorded.

The two methods are compared. It is concluded that translumbar needle aortography is simpler and less hazardous and should be the method of choice in all suitable cases.

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RETROGRADE AORTOGRAPHY WITH A SPECIAL CATHETER, INCLUDING DEMONSTRATION OF THE CORONARY ARTERIES*

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THE ROENTGENOGRAPHIC DEMONSTRATION of the heart chambers and the great vessels by means of the injection of radiopaque liquid into the venous system is now comparatively well established as a diagnostic procedure, particularly adapted to showing the right side of the heart and the lesser circulation. The radiopaque medium may be introduced by needle puncture or by venous catheterization. If local thrombosis occurs at the site of insertion of the catheter or injection of the opaque medium into the median basilic vein, which is usually used, or if this vein must be ligated or divided, no untoward symptoms occur. The injection is made with the blood current and against only a low pressure. The visualization of the left side of the heart and the thoracic aorta, however, have presented much more formidable difficulties.

The *abdominal* aorta and its branches have been demonstrated a great many times by the employment of various roentgenographic technics. In most cases this has been done by the direct trans-lumbar percutaneous puncture of the aorta with a large needle or trochar under general or spinal anesthesia, injecting the radiopaque medium under pressure, according to the technic of dos Santos.¹¹ The method carries with it the necessity of general or spinal anesthesia and the danger of injury to the artery or the surrounding structures. In very sick individuals these factors are of considerable importance. In 1941, Farinas,¹ displeased with his results with the dos Santos technic, reported roentgenographic delineation of the abdominal aorta and its branches by means of a rubber catheter introduced through a trochar into the femoral artery in Scarpa's triangle. Later, because of his inability to secure rubber catheters, he discarded this method in favor of "retrograde abdominal aortography,"²⁻⁴ a procedure in which 50 cc. of 70 per cent Diodrast is injected retrograde into the femoral artery in two and a half to three seconds by using 15 lb. pressure. The work of Farinas was concerned only with abdominal aortography.

The roentgenographic visualization of the *upper thoracic aorta* by direct percutaneous injection also has been reported. Radner¹⁰ found that he could visualize the ascending aorta and coronary arteries in dogs by direct injection

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into the aortic bulb. He then injected Thorotrast under fluoroscopic control into the proximal aorta of five human subjects by means of a trans-sternal needle puncture, obtaining delineation of the ascending aorta and faint outlines of the coronary vessels, although the superimposed shadows of the pulmonary veins interfered with the interpretation. As a result of the procedure, one patient developed mediastinal emphysema, another extravasation of blood into the pericardium and subsequent exudative pericarditis. Hoyos and del Campo⁶ injected 30 cc. of 70 per cent Diodrast solution in one second directly into the human aorta through an 18-gauge needle introduced through the second left interspace, obtaining ascending aortograms and light shadows of the coronary vessels. Grossman⁵ secured proximal aortograms in 12 dogs by injecting 25 cc. of 70 per cent Diodrast through a No. 10 wax catheter introduced through the right common carotid artery; the artery was ligated. The coronary arteries were demonstrated in the last five dogs. Several injections were done in each case using 100 to 150 cc. of Diodrast. All but one of the dogs died in which a successful coronary visualization was obtained. The roentgenographic identity of the coronary vessels was confirmed by repeating the injection after a non-



FIG. 1



FIG. 2

FIG. 1.—Dog with intact chest; lateral view, right side down. Special catheter was inserted to aortic sinus through left common carotid artery. The dog had stopped breathing, but the electrocardiogram still showed regular cardiac beats. There was no measurable pressure in the catheter. Four cc. of 70 per cent Diodrast were injected. The solution filled the left ventricle and aortic sinus, showing two cusps of the aortic valve and the origin of the left coronary artery. During this exposure the heart was not functioning as an efficient pump.

FIG. 2.—Dog with intact chest; lateral exposure, right side down. Special catheter was inserted through the left femoral artery to the aortic sinus. Four cc. of 70 per cent Diodrast were injected. The left circumflex, anterior descending and right coronary arteries, and some of their smaller branches, are well demarcated. One also sees the aortic sinus (Valsalva), the separate shadows of all three aortic cusps, and the ascending aorta.

L.A.D.—Left anterior descending coronary artery.

L. CIRC.—Left circumflex coronary artery.

RT.—Right coronary artery.

A.—Anterior cusp aortic valve.

R.P.—Right posterior cusp aortic valve.

L.P.—Left posterior cusp aortic valve.

constricting metallic loop had been placed around the anterior descending branch of the left coronary artery.

All of these technics had the following disadvantages: (1) large quantities of the radiopaque medium are used; (2) the arteriography is unnecessarily widespread and non-selective, thus confusing the interpretation, and (3) great force is used to inject the solution through comparatively small lumina (this does not apply to the catheter of Grossman), producing a sudden increase in intra-arterial tension which may injure or rupture a weakened arterial wall. To the author's knowledge, no satisfactory method for the roentgenographic demonstration of the proximal aorta has heretofore been reported.

For this purpose one of us (F. P.⁷) devised and reported a thin-walled radiopaque catheter which may be inserted into a peripheral artery and may be guided to any part of the aorta from the aortic sinus to the bifurcation of the abdominal aorta. The lumen transmits 5 cc. or more per second of liquid with simple manual pressure. The outside diameter (2.50 mm.) is small enough so that the artery of insertion may readily be restored by suture.



FIG. 3



FIG. 4

FIG. 3.—Dog with intact chest; oblique view, right side down. Special catheter was inserted into right carotid artery to aortic sinus. 25 cc. of 70 per cent Diodrast were injected. One sees well outlined the entire thoracic aorta and its branches, including vertebral, internal mammary and intercostal arteries. The amount of solution used is much too great for selective arteriography.

FIG. 4.—Dog, lateral projection, right side down. A special catheter was inserted through the femoral artery to the origin of the coeliac axis. Precision arteriography of the coeliac axis and its branches was done with 7 cc of 70 per cent Diodrast. Note the demonstration of the splenic, gastric, and hepatic arteries with their small branches. The inferior phrenic artery is also seen. The gallbladder has been visualized by previous injections of Diodrast.

The catheter was first used on dogs. By passing the catheter through the femoral or carotid arteries, it was possible to obtain arteriograms of any portion of the aorta with the use of small amounts of 70 per cent Diodrast. Satisfactory pictures were obtained of the left ventricle (Fig. 1), aortic valves (Figs. 1 and 2), coronary arteries (Fig. 2), proximal aorta, aortic arch and its main branches (Figs. 2 and 3). By placing the catheter tip at various levels in the descending aorta, the coeliac axis (Fig. 4), mesenteric arteries and renal arteries were demonstrated, showing minute branches in the stomach, liver, spleen, intestine, and kidneys.

Pearl, Friedman, Gray, and Friedman⁸ reported the regular roentgenographic demonstration of the coronary arteries in the intact animal by the use of 4 cc. of radiopaque liquid injected through the special intrarterial catheter

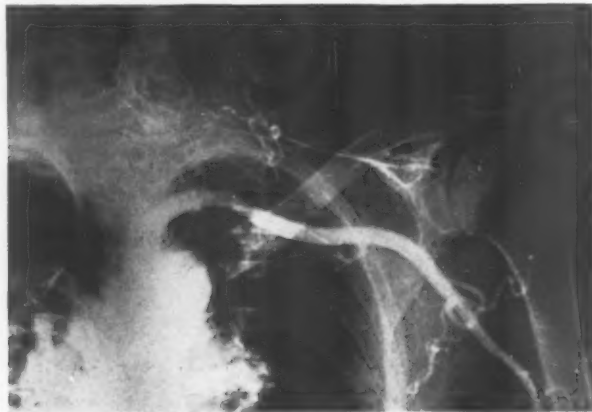


FIG. 5.—Human subject. A special catheter was inserted through the left radial artery to the proximal aorta. Ten cc. of 35 per cent Diodrast were injected. The proximal aorta, aortic arch, and subclavian and axillary arteries and their branches are well delineated. The radial pulse returned immediately following closure of the arterial wound of insertion.

by simple manual pressure on a Robb syringe. The left circumflex, left intraventricular, and right coronary arteries and many of their small branches were well delineated and showed good contrast. The method is safe and dependable. Electrocardiograms taken during the passage of the catheter, and during and after the injection of the radiopaque liquid showed no abnormality.

The catheter has been used in only one human subject. It was inserted through the left radial artery just below the brachial bifurcation and passed to the ascending aorta. Good arteriograms were obtained of the ascending aorta, aortic arch, and the left subclavian artery (Fig. 5). The artery was restored by suture and the radial pulse promptly returned at the wrist and has persisted. The segments of origin of the radial and profunda femoris arteries appear to be good sites for the insertion of the catheter, since their size is adequate to accom-

modate the catheter, and to allow of easy closure of the arterial defect. If thrombosis should inadvertently develop, no serious consequences would be likely to ensue. The femoral artery itself, and the radial artery at the wrist, if thrombosed, would be attended with a considerable risk of circulatory complications. In fact, gangrene has been reported when the radial artery was sacrificed at the wrist following intra-arterial blood transfusion.⁸ Because the ulnar artery gives off the important interosseous artery a short distance below its origin, this artery would be somewhat less desirable than the radial artery as the site of insertion of the catheter.

The technic for arteriography by arterial catheter is simple. The surgeon exposes a segment of artery and strips the adventitia from it. The blood flow is temporarily occluded by serrefines. An opening is made in the artery somewhat smaller than the diameter of the catheter. The latter is gently inserted into the artery. It is kept free of blood by connecting it to an apparatus which delivers through it, at a pressure just below systolic, a few drops per minute of heparinized normal salt solution. If leakage occurs, an arterial suture is necessary. The serrefines are removed and the catheter passed to the desired location. The angulated tip allows the catheter to follow the curve of the aortic arch.

The position is checked by fluoroscopy. If satisfactory, the roentgen ray apparatus is set for 1/20 second exposure, using the Bucky diaphragm, and the pressure apparatus is replaced by a 50 cc. Robb syringe containing the desired amount of radiopaque medium. From 4 to 10 cc. are sufficient, depending on the extent of the proposed visualization. The blood is kept from regurgitating through the catheter by manual pressure on the plunger. The operator makes certain that the catheter lies free in the aortic current and that the flow through the catheter is unobstructed. He then injects the solution as quickly as possible. By using a tunnel, two roentgen exposures are taken about one eighth to one fifth second apart, the first one about a half second after the injection has begun. After the fluid has been injected, the syringe is promptly replaced by the pressure apparatus. The films are developed and inspected. If unsatisfactory, further films may be taken, altering the position of the catheter, the amount of fluid, or the temporal relationship between injection and exposure. If the films are satisfactory, the catheter is withdrawn and the serrefines replaced. The operator makes sure that the artery is free of clots proximal and distal to the site of insertion of the catheter and closes the small opening with 6-0 arterial silk.

The arterial catheter delivers the radiopaque solution in high concentration at the exact location desired, permitting one to use small amounts of solution to obtain clearer and more detailed arteriograms. The use of small amounts of solution also allows a good contrast of the outlined vessels against a background not clouded by excess of opaque medium.

The use of the intra-arterial catheter offers a safe and dependable method for clear-cut and selective arteriography of regions previously not amenable to

satisfactory roentgenographic demonstration. This method has important implications in respect to the diagnosis and possible therapy of cardiovascular disorders in human beings, and to the conduct of cardiovascular research in man and animals. Through the catheter one may also obtain blood samples from selected sites, including the left ventricle. The catheter furnishes a method for studying the effect of various substances on selected organs, allowing the substance to be deposited in high concentration at localized areas.

SUMMARY

Until now no satisfactory method has been available for the roentgenographic demonstration of the thoracic aorta, especially its proximal portion. A special catheter was devised which can be inserted into a peripheral artery and can be guided under fluoroscopic control to any portion of the aorta and many of its larger branches. The catheter has an outside diameter small enough to permit restoration of the artery by suture (2.50 mm.), and a lumen large enough (0.59 mm.) to transmit 5 cc. of fluid per second by manual pressure. It allows one to take selective arteriograms of any portion of the aorta by using only a few cc. of radiopaque liquid. The coronary arteries may be regularly demonstrated by this method. The arteriograms thus obtained show excellent contrast, since the vessels visualized are not obscured by an excess of radiopaque medium. The number of reactions from the use of such small amounts of Diodrast will probably be markedly reduced; when reactions occur they will be much less severe and dangerous. The technic for use of the catheter is described. The intra-arterial catheter offers a safe and efficient method for the selective roentgenographic visualization of the proximal thoracic, arch, and descending thoracic aorta.

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MYOTOME AND SCLERATOME PAIN*

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MOST INJURIES heal completely, and typically become painless in due time. Some injuries progress atypically and give rise to persistent radiating pain—variously named minor causalgia, reflex sympathetic dystrophy, posttraumatic pain syndrome, or posttraumatic dystrophy. When such pain, as it frequently does, radiates across classic boundaries of the peripheral nerves, an aura of mystery or suspicion may become attached to the complaint. It does appear, however, that some instances of such pain can be explained on the basis of referred pain in bones, joints, ligaments, tendons, or muscles. Study of patients in the light of experimental findings concerning deep pain radiation is of clinical interest.

Minor causalgia, posttraumatic pain syndrome, reflex sympathetic dystrophy, and posttraumatic dystrophy have characteristics in common; they are painful conditions following relatively minor lesions without known nerve involvement but with disablement out of proportion to the injury. Sometimes they exhibit a vascular component and frequently they are relieved by sympathetic nerve block. Homans¹ states that minor causalgia is a neurovascular disorder and lists such changes as atrophy of bone, edema, paresthesia, and vasomotor dysfunction; he indicates that it is the same syndrome Livingston² calls posttraumatic pain syndrome. The basic feature is pain; and it is to be noted that the pain is "of an uncertain and varying character associated with numbness in the fingers, loss of grip, very slight edema, paresthesia to pin prick, atrophy of the skin, and often of the bones, coolness and cyanosis of the part, and all in an area supplied by one or several great nerves . . ." That there may be more than one condition in this description is recognized by Homans on the basis of the facts that some patients are relieved by local infiltration and some by repeated blocks of the sympathetic nerves. In Homans' description, pain is sometimes bright and burning or sometimes dull. Livingston² would limit the diagnosis of minor causalgia to those instances where relatively minor injuries are followed by burning pain and disability. By posttraumatic pain syndrome he means "a symptom complex characterized by severe pain and protracted disability following an apparently minor injury" where the pain is not burning but is dull and where the pain does not conform to definite peripheral nerve patterns. Posttraumatic pain syndrome is sometimes relieved

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by local injection of tender areas and sometimes by sympathetic block. Evans³ described reflex sympathetic dystrophy as a syndrome with the chief characteristic of agonizing burning pain, although he will allow the diagnosis in absence of pain if the additional distinguishing features are present: rubor, pallor, or both; swelling; sweating; and often cystic atrophy of bone. The causes are diverse but are mostly traumatic, often minor, and not of the nature which would be expected to result in persistent pain. Under the title post-traumatic dystrophy, Miller and de Takats⁴ describe a painful vasomotor and trophic disorder, indicating that it is much the same thing Homans calls minor causalgia. They have been concerned mostly with the vascular features and have examined changes in blood flow in these patients.

From consideration of the descriptions of minor causalgia and related states and from study of reported cases, it seems that patients fall into three groups: (1) some have burning pain; (2) some have vasomotor dysfunction predominantly; and (3) some have aching pain which transcends the boundaries of the dermatomes. It is this third group with which this discussion is primarily concerned.

The kind of pain which patients in the third group present can be described clearly. It is a deep ache, dull or severe, radiating from a site of injury for a greater or lesser distance and overlapping skin nerve boundaries. It is accompanied by a feeling of weakness and disability out of proportion to the injury which produces it. Moreover it is usually accompanied by a subjective sensation of numbness; occasionally there is hyperthesia of the skin. It is the kind of pain Lewis⁵ calls muscle pain. When dull it is not very annoying and does not carry the same emotional overtone as neuritic or skin pain, which may account for the remarkably cheerful demeanor of some patients who suffer it. Not infrequently a patient describes it as "numb" pain. When first experienced it seems to be diffuse, but both experimentally and clinically the limits can be defined with considerable reproducibility. Far from being rare or unusual, this kind of pain is suffered several times daily by some patients who receive intramuscular injections of irritating substances; a few years ago certain batches of penicillin were notorious in this respect. Anyone who has never done so may readily experience momentarily this type of pain through the expedient of injecting 5 per cent saline into one of his own muscles. At the same time he may also observe, if he has a labile vasomotor system, transient vasomotor changes in the affected extremity similar to those seen in clinical posttraumatic pain states.

The experimental observations which deal with this type of pain are those of Kellgren.⁶ After Lewis⁵ showed that the quality of pain from somatic structures depends more on the structure stimulated than on the kind of stimulus, and after he had also noted wide and apparently unanatomic pain radiation from muscles, Kellgren undertook a systematic study in which hypertonic saline was injected into muscles of a number of normal subjects. Using repeated injections and trained observers he established the fact that, within

MYOTOME AND SCLERATOME PAIN

narrow limits, stimulation of a given muscle at the same site gives rise to a characteristic pattern of pain radiation. The region of radiation was found to correspond to the spinal segments from which the motor innervation of the muscle is derived, this distribution being somewhat different from the arrangement of the dermatomes. Figure 1 B illustrates radiation of pain observed from injection of 1 cc. of hypertonic saline into the brachioradialis muscle. The constancy with which a pattern can be reproduced was noted by Kellgren and again demonstrated in our subjects.

Observations pertinent to radiation of somatic pain have been made by Inman and Saunders.⁷ These investigators carried out studies on pain radiation from bone and periosteum principally, using the same method as Kellgren.

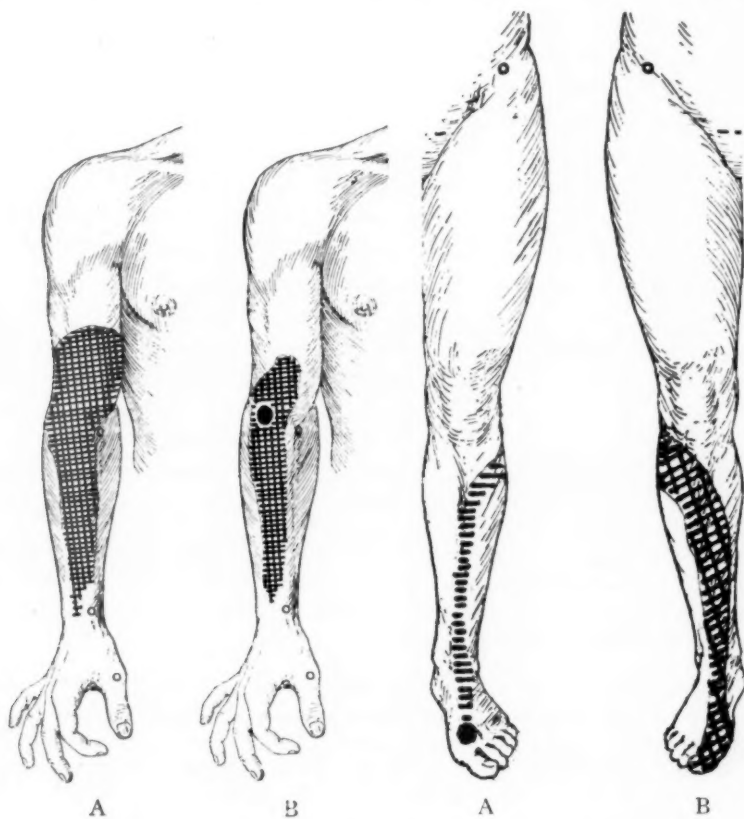


FIG. 1

FIG. 2

FIG. 1.—Pain radiation in minor causalgia. A illustrates the distribution of pain experienced by Case 1. B is the characteristic pattern of pain radiation from injection of hypertonic saline into the origin of the brachioradialis muscle. The diagrams in these illustrations do not depict anesthesia, hypesthesia, or any other surface phenomenon. They are approximations of the radiation of deep pain sensibility about an injury or stimulus.

FIG. 2.—A illustrates the distribution of pain experienced by Case 2. B, taken from Inman and Saunders, is an approximation of one of the scleratomes.

They established the segmental character of pain radiation from skeletal structures again in arrangements frequently dissimilar to dermatomes. These patterns they aptly termed scleratomes. Figure 4 B shows two scleratome patterns. The description of pain produced in their subjects agrees closely with that of deep pain described by Lewis and the pain described by our patients cited below. It is interesting to note that Inman and Saunders found this pain to be associated with vasomotor phenomena such as nausea, vomiting, sweating and peripheral vasoconstriction.

It is instructive to examine patients with atypical or radiating disabling pain in the light of these experiments. While criteria for diagnosis of minor causalgia and related states are not explicit, a group of 26 individuals were seen who appeared to fit into this category. The common characteristics include: radiating, aching pain spreading beyond the distribution of peripheral nerves; considerable weakness and disability in the affected extremity; minor injuries without clinically acceptable evidence of damage to nerves. Some had edema and in some there was pallor or rubor and excessive sweating. When the disability was of long standing, some had bony atrophy. Twenty-two of the 26 were relieved of their symptoms at least temporarily by sympathetic nerve block; in nine of 12 in whom it was tried, symptoms were relieved by tetraethylammonium chloride. The patterns of pain radiation in these patients fitted patterns of pain radiation described and illustrated by Kellgren⁶ or Inman and Saunders⁷ or fitted patterns established in normals through extension of their experiments. Brief descriptions of the courses of several illustrative patients follow.

Case 1.—This patient, a 36-year-old white male, was injured when he slipped, fell, and struck the lateral aspect of his right elbow. After a few days acute pain subsided, leaving dull aching pain in the distribution shown in Figure 1A. In addition to pain he had loss of grip and loss of strength so that he could not work more than half an hour without resting. Vasomotor disturbances were absent. His symptoms were relieved temporarily by sympathetic ganglion block, T1 and T2. He became asymptomatic, without any particular treatment, four months after the injury.

Case 2.—This 23-year-old white man shot himself accidentally through the right foot with a .22 rifle; he sustained a through and through wound with fracture of the first metatarsal. When first examined, one year after injury, he presented a complaint of pain radiating as shown in Figure 2A. The pain was not always present, but was brought on by trauma to the scar of the plantar surface, such as from climbing an iron ladder, and by change in weather. Such an attack of pain lasted a week or more and was associated with a sensation of numbness in the whole foot, with mottled cyanosis of the skin and with excessive sweating. Ever since the injury the right foot had felt stiff, even without pain being present. Sympathetic ganglion block, L1 and L2, brought about temporary relief of pain but no lasting improvement. When last seen his symptoms persisted unabated; further treatment is planned.

Case 3.—This young man cut the end of his thumb to the bone; the resulting scar, dividing the end of the distal pad of the thumb, was sensitive to touch. During the winter when he had to expose his hands to cold, he experienced pain after moderate exposure in the distribution shown in Figure 3A. During these episodes he had weakness of the

MYOTOME AND SCLERATOME PAIN

extremity, at times quite marked, but he exhibited no visible vasomotor phenomena. Over the course of a year he improved spontaneously.

Case 4.—This 37-year-old white man injured his right index finger when he accidentally stuck a thumb tack into the distal interphalangeal joint. At once the finger became swollen and exquisitely painful but remained cool and pallid and did not respond to treatment for infection. No suppuration or inflammation was ever demonstrated but the finger and eventually the hand became edematous, pale, and sweated excessively. Six months after injury, when the symptoms were at their height, he described pain radiating as shown in Figure 4A, associated with a feeling of numbness and great weakness in the entire extremity. Thoracic ganglion blocks, T1 and T2, or T1, T2, T3, and T4, repeated on several occasions, did nothing toward relieving his pain even temporarily. Gradually his symptoms subsided spontaneously. Eighteen months after injury he experienced at times only local pain in the finger. By this time, also, swelling had disappeared as had the symptoms of weakness and numbness.

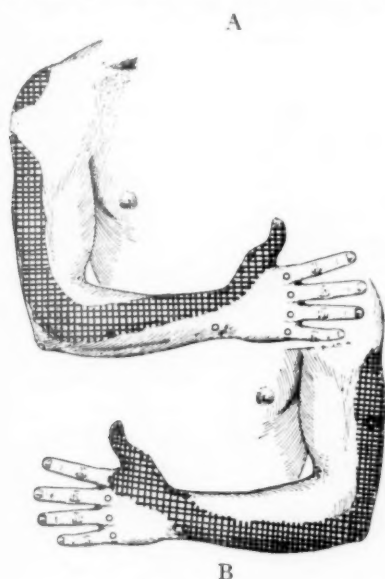


FIG. 3

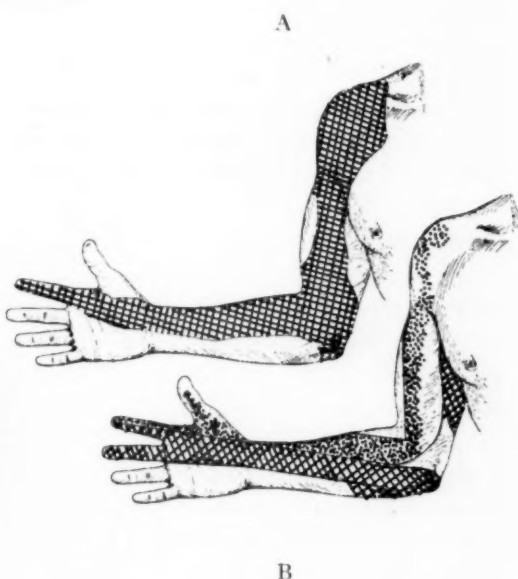


FIG. 4

FIG. 3.—A illustrates distribution of pain experienced by Case 3. B, taken from Kellgren, illustrates the characteristic pattern of pain radiation from injection of hypertonic saline into the adductor pollicis longus.

FIG. 4.—A illustrates the distribution of pain experienced by Case 4. B, taken from Inman and Saunders, is an approximation of two of the scleratomes in the upper extremity.

In some of our patients the exciting cause of pain has been apparent, as in Cases 2 and 3, where visible scars remain. In two others, removal of small diffuse fibrous masses overlying the lateral epicondyles of the humeri resulted in cure. In one with radiating forearm centered at the wrist, a fibrocartilagenous mass 3 mm. in diameter was removed successfully from the posterior aspect of the triangular bone of the wrist—the site of a fracture 17 months old—in the face of normal roentgenograms of the joint. Preoperatively this patient exhibited ulnar nerve hypesthesia and coldness of the little finger; it is

curious that these changes have been relieved by the operation. An exciting cause of pain could be demonstrated in 15 of 26 patients. The inference seems clear that some patients who might well be considered to exhibit minor causalgia do in fact exhibit somatic pain radiation arising from injury. Interpretation of such complaints as examples of perfectly normal and experimentally reproducible pain radiation removes some of the obscurity which has frequently surrounded this subject.

Some clinical aspects of myotome and scleratome pain remain obscure. Thus the reason some scars produce radiating pain while most do not is unexplained. Why such pain should be favorably influenced in some instances by sympathetic block, ganglionectomy, or tetraethylammonium bromide is far from being completely clear, particularly in some patients where there is no visible evidence of vasomotor dysfunction. The most striking example of vasomotor dysfunction in our group (Case 4) obtained no benefit by such treatment. Kellgren⁸ has found deep pain sensibility to be peculiarly susceptible to cooling and attributes improvement by sympathectomy to abolition of reflex vasoconstriction and thus to cooling. Several experiments we have designed to elucidate this question have been unenlightening.

Not all instances of minor causalgia can be explained as myotome or scleratome pain radiation after injury. If the conclusions of Lewis⁹ are correct, those who have burning pain have had injuries to the skin or to nerves with skin sensory fibers. While vasomotor reactions in conjunction with somatic pain have been described experimentally and seen clinically, vasomotor disorders were not prominent in our group of patients. Those present were variable and frequently associated with examination or manipulation; if any exhibited sustained vasodilatation we did not detect it. Neither are all instances of radiating somatic pain found after injuries. In one discussion, Kellgren¹⁰ cites the clinical implication of his experimental work in relation to fibrositis or myalgia. (He also includes two patients in whom trauma appeared to be a precipitating factor.) Inman and Saunders⁷ recorded the nature, degree, and direction of pain radiation in a number of patients in addition to their experimental subjects and noted that scleratome patterns were observed after injuries, tenovaginitis, bursitis, scalenus anticus syndrome, osteoid osteoma, and metastatic carcinoma in bone.

SUMMARY

A striking resemblance exists between experimentally produced deep pain and the pain in some instances of minor causalgia. Consideration of such cases in the light of the experiments of Kellgren and of Inman and Saunders is of value in diagnosis and treatment.

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STATEMENT OF THE OWNERSHIP, MANAGEMENT, AND CIRCULATION REQUIRED BY THE ACT OF CONGRESS OF AUGUST 24, 1912, AS AMENDED BY THE ACTS OF MARCH 3, 1933, AND JULY 2, 1946 (Title 39, United States Code, Section 233) OF ANNALS OF SURGERY, published monthly at Philadelphia, Pa., for October 1, 1950.

State of Pennsylvania }
County of Philadelphia } ss.

Before me, a Notary Public in and for the State and county aforesaid, personally appeared J. R. Arnold, who, having been duly sworn according to law, deposes and says that he is the Treasurer of the ANNALS OF SURGERY and that the following is, to the best of his knowledge and belief, a true statement of the ownership, management (and if a daily paper, the circulation), etc., of the aforesaid publication for the date shown in the above caption, required by the Act of August 24, 1912, as amended by the Act of March 3, 1933, embodied in section 537, Postal Laws and Regulations, printed on the reverse of this form, to wit:

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[Signed] J. R. ARNOLD.

Sworn to and subscribed before me this 29th day of September, 1950.

[Seal]

HARRY J. BEARD.

(My commission expires March 5, 1953)

THE SURGICAL ASPECTS OF CALCIFIED HILAR LYMPH NODES*

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IN A REVIEW OF THE LITERATURE, it has been noted that only seldom are clinical symptoms attributed to benign hilar lymphadenopathy; no reports are presented of the establishment of a syndrome whereby surgical intervention has been necessary to bring about a cure.

The author feels that insufficient emphasis has been placed upon the importance of calcified hilar lymph nodes with the resulting clinical manifestations of extrinsic bronchial compression and bronchial erosion; in other words, the importance of their physical presence. The chief clinical manifestations, as noted by personal observation, have been: (1) partial bronchial obstruction with persistent wheezing; (2) partial or complete bronchial obstruction with the subsequent development of atelectasis, fibrosis, and infection which in turn produces cough, sputum and hemoptysis; (3) bronchial erosion producing cough, sputum, hemoptysis and broncholiths; and (4) endogenous spread of tuberculosis due to the intrabronchial rupture of tuberculous lymph nodes, with subsequent aspiration pneumonia, hematogenous spread, and miliary tuberculosis.

The intrabronchial rupture of a caseous lymph node is considered to be one of the main modes of progression of a primary tuberculous process.¹ However, due to the low incidence and the fulminating course when it occurs, it is not a surgical problem. The other manifestations have been noted on numerous occasions, and eight of the more typical examples are presented. In all cases the patients presented themselves with definite symptoms; in every case evidence was found to substantiate the cause as being due to compression or erosion of a bronchus by calcified hilar lymph nodes.

Case 1.—P. H., a 48-year-old white female, entered the hospital complaining of a persistent cough of 4 years' duration. Roentgen ray examination (Fig. 1) revealed a shadow in the mid-portion of the right lung field, and bronchography revealed a block in the right middle lobe. Bronchoscopy was negative and a bronchial lavage examination was negative for tumor cells.

The chest was explored and an inflammatory mass was found in the right middle lobe. A biopsy was negative for cancer, so a lobectomy was performed. During the hilar dissection, numerous calcific deposits were found about the middle lobe bronchus. On cutting the bronchus, it was noted that the proximal portion was almost totally obstructed due to extrinsic pressure from calcified lymph nodes. These lymph nodes were dissected free and the bronchus severed close to its origin.

The patient made an uneventful recovery and is now symptom free.

The pathologic report revealed bronchiectasis, chronic fibrosing pneumonitis, and calcified lymph nodes.

Comment. This patient presented the problem of a history of cough; roentgen ray evidence of segmental atelectasis and definite evidence of a block to

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a segmental bronchus by bronchography. Bronchoscopy was negative, and the exploratory operation was undertaken on the assumption that a tumor was probably present—most likely a bronchogenic carcinoma. At operation the diagnosis of bronchiectasis was made; the obstruction in the bronchus was demonstrated to be due to extrinsic pressure from calcified lymph nodes encircling the bronchus. Surgery has produced a satisfactory result.

Case 2.—G. H., a 35-year-old white female, entered the hospital complaining of cough, wheezing, and expectoration of 2 years' duration. Roentgen ray examination (Fig. 2) revealed numerous calcific deposits in the right lung involving the middle and perhaps lower lobes. Bronchography disclosed no evidence of bronchiectasis. The patient was bronchoscoped and a proliferative lesion was found partially obstructing the right middle lobe bronchus. Biopsies were taken and revealed only chronic inflammatory tissue. In view of the persistent symptoms and obstructing lesion, a lobectomy was proposed. At operation, multiple large caseous and calcified lymph nodes were found surrounding the right middle and lower lobe bronchi. The lower and middle lobes were resected and the involved lymph nodes removed. The obstructing granulation tissue at the origin of the middle lobe bronchus was the site of erosion of one large calcified lymph node.

The patient made an uneventful recovery and is symptom free.

The pathology report was patchy atelectasis, fibrosis, chronic bronchitis, caseous and calcified tuberculous lymph nodes.

Comment. While this patient presented no emergency, she did pose quite a problem in producing relief of her symptoms. The resulting picture found at surgery justifies the approach taken. It is interesting to speculate upon the possibility that this patient, without surgical intervention, might eventually have developed a tuberculous pneumonia, due to the eroding tuberculous lymph node. Unfortunately, at the time, bacteriologic studies were not carried out. However, Opie and Aronson,² found living tubercle bacilli in 0 to 33 per cent of all lymph node foci and in 20 per cent of all calcified focal lesions. Even though one minimizes the danger of endogenous tuberculous infection, the presence of progressive constriction and erosion of the bronchus, and obstruction due to granulation tissue would eventually have led to destructive parenchymal changes, and the surgical approach seems justified.

Case 3.—S. J., a 46-year-old white female, entered the hospital complaining of a slight cough and hemoptysis of one year's duration. Roentgen ray examination (Fig. 3) revealed an area of increased density in the region of the right middle lobe. Bronchography was negative. Bronchoscopy was negative. Sputum and bronchial lavage examinations were all negative for acid fast bacilli and tumor cells. In view of the cough and hemoptysis of one year's duration, and an unexplained shadow on roentgen ray examination, an exploratory thoractomy was performed. At operation, an atelectatic right middle lobe was found, and the bronchus was surrounded and almost completely compressed by calcified lymph nodes. The involved nodes and middle lobe were removed. The patient recovered and is now symptom free.

The pathologic report was chronic bronchitis, bronchiectasis, areas of pneumonitis, atelectasis, and calcified lymph nodes.

Comment. The problem here was an unexplained pulmonary shadow with a history of a year of cough and hemoptysis. The patient was explored for the

FIG. 1

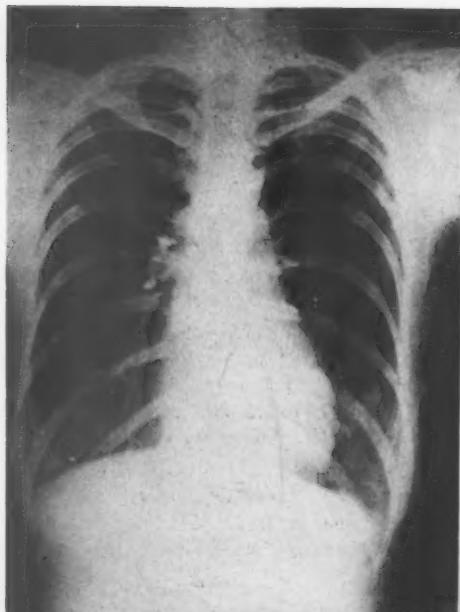


FIG. 2

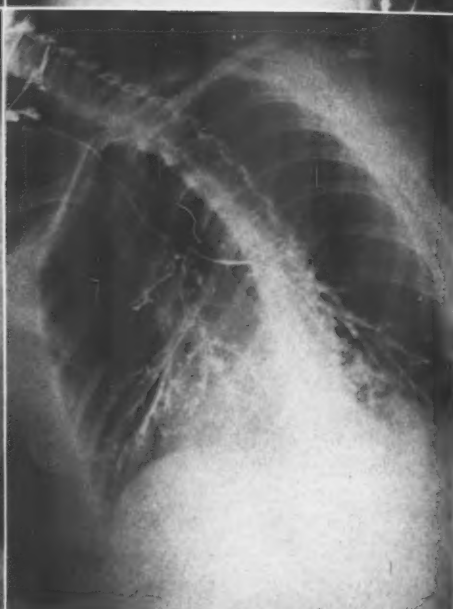


FIG. 3

FIG. 4

FIG. 1.—(Case 1) Roentgenogram demonstrating shadow in the mid-portion of the right lung field. The calcific deposits are visible in the right hilar region.

FIG. 2.—(Case 2) Roentgenogram demonstrating calcific deposits in the right lung field.

FIG. 3.—(Case 3) Roentgenogram demonstrating a shadow in the right mid-lung field. The calcific deposits are also visible.

FIG. 4.—(Case 4) Bronchography demonstrating an obstruction in the right common bronchus. Some of the calcific deposits are visible adjacent to the right common bronchus.

possibility of cancer, and early suppurative lung disease secondary to bronchial obstruction was found; the obstruction apparently being due to extrinsic pressure from calcified lymph nodes.

Case 4.—M. L., a 50-year-old white female, entered the hospital complaining of cough, hemoptysis, and wheezing of one year's duration. The patient had previously been diagnosed as having intrinsic asthma. Therapy to date had been to no avail. Physical examination revealed marked lack of aeration and numerous ronchi throughout the right chest. Roentgen ray examination was essentially negative. Bronchography (Fig. 4) revealed an obstructive lesion in the right common bronchus. The patient was bronchoscoped and a proliferative mass, almost obstructing the right common bronchus, was found. A biopsy was taken and the report was papilloma of the bronchus. The entire tumor, as visible in the bronchus, was removed and the patient's symptoms disappeared. However, they soon re-appeared, and during the next 2 months the patient was bronchoscoped 3 times. Each time a considerable amount of tumor tissue was removed with subsequent relief of symptoms. All biopsies were reported as papilloma of the bronchus. Even though all biopsies were reported as benign, it was feared that the tumor was actually malignant. If actually benign, the bronchial obstruction, persistent symptoms and repeated bouts of hemoptysis justified surgery. At operation the right common bronchus was found to be almost surrounded by a mass of calcified lymph nodes. A pneumonectomy had to be performed to remove the involved area, and the hilar dissection was extremely difficult due to the numerous calcified lymph nodes. The patient made an uneventful recovery and is now free of symptoms.

The pathologic report revealed a calcified Ghon tubercle with calcified hilar lymph node tuberculosis; atelectasis; pneumonitis; chronic bronchitis with a typical papillary hyperplasia and squamous metaplasia of the bronchial epithelium; and at one area there was pseudo papillary formation. This area of squamous metaplasia and papillary hyperplasia was located in the right common bronchus which was externally compressed by calcified lymph nodes; the base of the pseudo papillary formation was the site of erosion through the wall of the bronchus by the underlying calcified focus.

Comment. This patient, originally diagnosed as an asthmatic, proved to have a tumor producing obstruction of the bronchus. Although all biopsies were reported as benign, the very location of the tumor and symptoms produced made it clinically a malignant process. Because of the fear of a pathologic malignancy beyond reach of the biopsy forceps, a pneumonectomy was performed. The true nature of the pathologic condition was demonstrated at operation to be due to compression and erosion of the common bronchus by a calcified lymph node with resulting squamous metaplasia and papillary hyperplasia.

Case 5.—N. D., a 37-year-old white male, entered the hospital as an emergency case due to massive hemoptysis. The patient had had a cough and expectoration of 6 years' duration. There had been numerous examinations, chest roentgenograms, and bronchoscopies in the past, but all were reported as negative. Chest roentgenograms at this time revealed an area of increased density in the right lower lung. The patient was bronchoscoped, and blood was found coming from the right lower lobe bronchus. The patient continued to have frequent, frank hemorrhages; after preliminary blood transfusions, an exploratory thoracotomy was performed. At operation a very large series of partially calcified lymph nodes were found surrounding and obstructing the right middle and lower lobe bronchi. After a great deal of tedious dissection, the lymph nodes were removed so

that a resection of the middle and lower lobes could be performed. The patient recovered and is now symptom free.

The pathologic report was fibrosis, bronchiectasis, chronic interstitial pneumonitis, and calcified lymph nodes.

Comment. This patient had an unexplained pulmonary shadow, and uncontrolled hemoptysis. Thinking a tumor was probably present, and in view of the persistent bleeding, the chest was explored; bronchiectatic middle and lower lobes were found with calcified hilar lymph nodes producing an extrinsic bronchial obstruction.

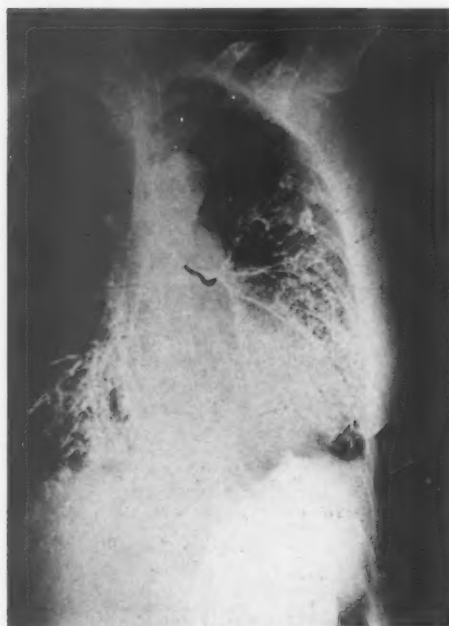


FIG. 5

FIG. 5.—(Case 6) Bronchography showing a block in the left lower lobe bronchus with atelectasis.

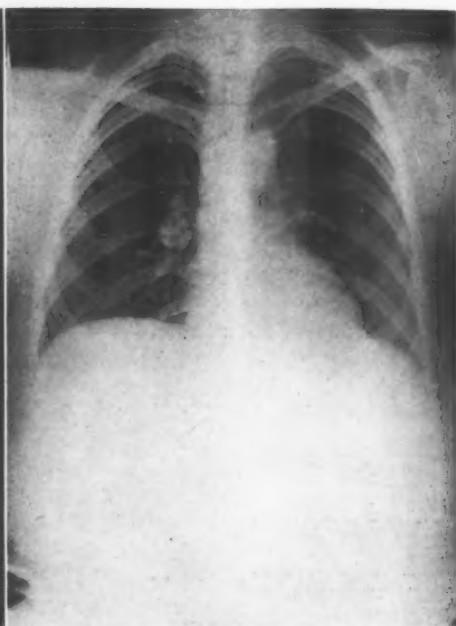


FIG. 6

FIG. 6.—(Case 7) Roentgenogram demonstrating a large calcific deposit in the right root region.

Case 6.—B. H., a 62-year-old white female, entered the hospital complaining of cough and wheezing of about 14 years' duration. During the past 8 months the cough had become productive. Recently, hemoptysis had been frequent and copious. Physical examination was negative. Sputum examinations were negative for acid fast bacilli. A chest roentgenogram was negative. The patient was bronchoscoped and there appeared to be complete blockage of the left lower lobe bronchus. Examination of a bronchial lavage was negative for tumor cells. A bronchography (Fig. 5) revealed a block in the left lower lobe bronchus with atelectasis; the upper lobe filling the entire chest. On the fourth hospital day the patient had a profuse hemoptysis. A repeat bronchoscopy showed blood coming from the left lower lobe bronchus. The patient was prepared for operation, and an exploratory thoracotomy was performed. An atelectatic left lower lobe was found, and the bronchus found to be surrounded and almost completely obstructed by a mass of calci-

SURGICAL ASPECTS OF CALCIFIED HILAR LYMPH NODES

fied lymph nodes. The lymph nodes were dissected free and a lobectomy performed. The patient recovered and is now symptom free.

The pathologic report was atelectasis, fibrosis, bronchiectasis and calcified lymph nodes.

Comment. This patient presented the problem of unexplained hemoptysis. The only positive finding was a block in the left lower lobe bronchus by bronchography. At exploration, a bronchiectatic lobe was found caused by an extrinsic bronchial obstruction from calcified lymph nodes.

Case 7.—R. K., a 44-year-old white female, complained of cough, some hemoptysis, and spitting up broncholiths of 6 months' duration. Physical examination was negative. Roentgen ray (Fig. 6) revealed a large calcified lymph node in the right hilar region. Complete bronchography was negative. Bronchoscopy disclosed a proliferative lesion in the right common bronchus. Biopsy revealed chronic inflammatory tissue. All sputum studies were negative for acid fast bacilli.

This patient has refused operation, but has been followed for about 3 years. Symptoms have persisted, and repeated bronchoscopies have revealed granulation tissue in the right common bronchus with all biopsies being negative for tumor cells.

Comment. Due to the similarity to the cases proved at operation, this patient is presumed to have an erosion of the bronchus from a calcified lymph node, resulting in chronic bronchitis, bronchial obstruction, hemoptysis, and production of broncholiths. It is felt that this patient will eventually develop all the sequelae of bronchial obstruction and that only surgery can produce a cure.

Case 8.—C. L., a 35-year-old white female, complained of cough for 4 years and a recent attack of hemoptysis. Complete examination was negative except for an area of calcification at the base of the right middle lobe. The diagnosis of tracheobronchitis with possible bronchial erosion was made. This patient has subsequently been followed for 5 years with persistence of cough, increasing frequency of hemoptysis and the most recent bronchography shows bronchiectasis of the right middle lobe.

Comment. It is now presumed that this patient likewise has slow progressive bronchial obstruction due to calcified lymph nodes, and also some erosion. She is slowly developing pulmonary changes characteristic of partial bronchial obstruction and it is felt that eventually surgery will have to be performed to produce a cure.

DISCUSSION

There are several causes for the production of benign calcified hilar lymph nodes, the classical one being tubercle formation during a primary tuberculous complex. However, it is not the intention of the author to discuss the mechanism of formation of the calcified lymph nodes, or the etiologic factors concerned. The object of this paper is simply to bring out the mechanical influence of such existing lesions upon the pulmonary tree. While it is felt that these ideas have been intimated, they have certainly not been emphasized in the literature, especially from a surgical standpoint.

It would seem likely that the presence of these large calcified lymph nodes

in the hilar regions would produce more frequent symptoms than ordinarily observed. In 1920, Eliasberg and Neuland³ first described large, usually lobar shadows in the chest roentgenograms of tuberculin-positive children whose clinical condition was astoundingly good in comparison with the roentgen ray findings, which were suggestive of a tuberculous pneumonia. These children have few if any symptoms. After a few months, the shadow clears, and leaves roentgenologically normal parenchyma. Several different theories have been proposed in explanation of this morbid entity.

Clinical, bronchoscopic, and pathologic observations have produced evidence that at least some, and probably most of the cases, are caused by bronchial obstruction with the parenchymal changes consequent to it. This, of course, explains the mildness of the symptoms and the uneventful clearing when the bronchial obstruction disappears. To this clinical entity has been attached the name of "epituberculosis." The cause of obstruction has been found to be pressure of large caseated lymph nodes of the primary complex, caseous material from primary lesions within the bronchus, tuberculous granulation tissue or calcified foci within the lumen of the bronchus. The final result frequently is not simple atelectasis. In the late stages mild or massive fibrosis of the involved lobe is frequent. Just as in other forms of bronchial obstruction, uncomplicated atelectasis is rare, although the secondary changes may be clinically insignificant.

Thus it would seem that a reasonable explanation is at hand for the course of events in the case reports presented: the symptoms being most reasonably explained on the basis of long standing, progressive compression of the bronchus, and eventual erosion and obstruction of the involved bronchus with their characteristic sequelae. These calcified lymph nodes are benign, *per se*, but their specific location and the subsequent chain of events leading to erosion hemorrhage and obstruction, both intrinsic and extrinsic, with resulting atelectasis, fibrosis, infection and parenchymal destruction make them clinically malignant.

The author feels that insufficient importance has been attached to the presence of these calcified hilar lymph nodes. The relatively high incidence of exposure to tuberculosis in the general population, as evidenced by the positive tuberculin test, is an indication of the frequent occurrence of at least one type of calcified hilar lymph node. The personal observation of numerous cases of bronchial erosion and compression, secondary to these lymph nodes, would seem to indicate their relatively common role as cause of clinical manifestations, including cough, sputum, wheezing, hemoptysis, and broncholiths. Their physical presence causing erosion and obstruction, with the attendant suppurative lung disease distal to the bronchial obstruction, makes them truly of surgical significance. In addition to the suppurative lung disease found in the cases presented, a more serious manifestation was immediately presented by four of the cases in the form of a questionable neoplasm, and in one of the cases by serious hemoptysis, both demanding prompt surgical attention.

SUMMARY

1. Eight typical cases have been presented demonstrating the surgical significance of calcified hilar lymph nodes. While others have also been observed, these have demonstrated rather clear-cut evidences of being due to the physical presence of calcified lymph nodes. Some of these lymph nodes have been located in the pulmonary parenchyma, but most were somewhere near the hilus.

2. The chief diagnostic findings were roentgen ray evidence of isolated lymph nodes which were partially calcified; areas of inflammatory change surrounding the lymph nodes or distal to them; and areas of atelectasis distal to these lymph nodes. Endoscopy was of value in certain cases and is an indispensable diagnostic procedure. Bronchography was perhaps of the greatest value in localizing the process.

3. The differential diagnosis was frequently not possible until an exploratory thoracotomy had been performed; however, an impression can be formed when the mechanism of this condition is borne in mind. Bronchogenic carcinoma has to be considered in this type of case in view of the clinical and diagnostic findings.

4. The chief pathologic findings were bronchial erosion, bronchial constriction, atelectasis, fibrosis, and suppuration. In every case evidence was present demonstrating the causative lesion to be calcified hilar lymph nodes.

5. The author feels that in the past little importance has been attached to these lymph nodes. While usually they are clinically benign, they may be the causative agents of very serious pulmonary disease. It is felt that they are frequent, and if their significance is appreciated, the importance of their surgical aspects will be apparent. Fortunately, in a high percentage of cases, surgery gives relief of the above mentioned pulmonary complications.

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THE SURGICAL SIGNIFICANCE OF ACANTHOSIS NIGRICANS*

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ACANTHOSIS NIGRICANS is a relatively rare cutaneous disorder whose existence has long been recognized in dermatologic literature but of which little has been mentioned in other medical publications. This in itself would not bear comment except for the very significant fact that in approximately 50 per cent of these patients there is sooner or later associated cancer, usually abdominal in origin. Hence, to the practicing physician the diagnosis of acanthosis nigricans, especially in the older individual, is of serious prognostic import and is an absolute indication for a thorough investigation of the patient.

Clinically, acanthosis nigricans is characterized by the appearance of soft, velvety, brownish-to-black, verrucous plaques typically in the cutaneous folds, involving chiefly the axillae, external genitalia, perianal region, nipples, umbilicus and angles of the mouth. The mucous membranes may also be affected. Hyperkeratosis of the palms and soles and papillomatous elevations in other areas may be present. There is often hair loss in the affected parts.

Recognition of acanthosis nigricans as a clinical entity was first reported independently by Pollitzer¹ and Janovsky² in the same volume of the International Atlas of Rare Skin Diseases in 1890. Since that time, over 420 cases have been listed in the literature, almost entirely in dermatologic publications.³ Comprehensive reviews of the subject have been written by Mukai,⁴ Moncorps,⁵ and most recently by Curth.⁶ Without much doubt many more patients with this disease have been seen without having the dermatosis identified.

Because of the association in approximately half of all cases of acanthosis nigricans with malignant tumors, two varieties are described, the benign (juvenile) and the malignant (adult) types. Typically the non-malignant form of acanthosis nigricans occurs in young individuals and may be present at birth, or appear early in life or at puberty. The malignant type more often manifests itself after the age of 40. However, a significant number of instances of malignant neoplasm in younger patients with acanthosis nigricans has been reported, so that no hard and fast rule can be made. The cutaneous findings in both varieties of the disease are practically identical clinically and histologically, and cannot be differentiated. Both sexes are equally affected.

The site of the neoplasm in the adult type of acanthosis nigricans is almost always abdominal. Curth⁶ in an analysis of 191 patients with acanthosis nigri-

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cans associated with tumors found that 93 per cent of the malignant lesions were abdominal and seven per cent thoracic in origin. In 70 per cent of the patients of the former group the neoplasm was located in the stomach. Other sites recorded are the uterus, liver, rectum, intestine and ovary. Extra-abdominal tumors have included carcinoma of the breast, lung and mediastinum. By far the most frequent type of carcinoma has been adenocarcinoma. Sarcoma and lymphosarcoma are also reported. The tumors are, as a rule, highly malignant. The onset of the cutaneous lesions and the tumor is often concomitant, although the cutaneous manifestations usually will precede the actual diagnosis of the neoplasm by several months. However, cases are reported in which the cutaneous findings were present for a number of years before the malignant growth became evident. In rare instances the eruption has been observed to appear subsequent to surgical treatment or irradiation of the tumor.

ETIOLOGIC CONSIDERATIONS

Various theories have been propounded in the past in an attempt to explain the cause of acanthosis nigricans, none of which has been entirely satisfactory. Darier⁷ originally hypothesized that the cutaneous changes were due to the mechanical action of the tumor tissue directly on the abdominal sympathetic nerves or adrenal glands. He also suggested that the neoplasm might be producing a toxin which affected the sympathetic nervous system leading to the changes of acanthosis nigricans. However, neither of these theories has explained the appearance of the lesions in the benign form of acanthosis nigricans. Also, at autopsy in the malignant type, the sympathetic nerves and adrenal glands are often found uninvolved by the tumor.

The association of the benign type of acanthosis nigricans with endocrine disturbances has been noted by a number of investigators. However, since no one type of glandular change has been consistently recorded, these endocrine changes are unlikely to be a causative factor.⁸

Confusion of acanthosis nigricans with Addison's disease is understandable in view of the somewhat similar cutaneous alterations. In both, the chromaffin system apparently is affected, which accounts for the pigmentary changes. Likewise hyperpigmentation occurs essentially at sites in which pigmentation is normally increased, in the flexural folds, especially the axillae, groin, perianal region and umbilicus.⁸ The mucous membrane surfaces are more commonly involved in the Addisonian syndrome. However, in the latter, increased melanin deposition is more apt to be seen at points of friction and exposure, the texture of the skin is normal, and most important, there is absence of the hyperkeratotic, verrucous and papillomatous lesions which are characteristic of acanthosis nigricans. Of course, from the internal aspect, Addison's disease can be distinguished by the typical findings of progressive asthenia, low blood pressure, anorexia, weight loss and an intolerance to sodium restriction; but it is easy to see how, in the absence of thorough investigation, acanthosis nigricans associated with abdominal malignancy could be mistaken for true Addi-

son's disease. As a matter of fact one of Addison's original cases, as described, was without much question one of acanthosis nigricans associated with gastric neoplasm.^{3,9}

Another interesting observation is the frequent finding of a familial history of malignant neoplasm in patients with acanthosis nigricans, in both the benign and malignant types. Curth⁶ has interpreted this fact as evidence of the genetic relationship between acanthosis nigricans and neoplasm. She considers the



FIG. 1



FIG. 2

FIG. 1.—This shows typical soft, velvety verrucous, hyper-pigmented, confluent plaques in the left axilla.

FIG. 2.—This demonstrates typical discrete warty lesions, and also irregularly distributed mottled macular areas of hyper-pigmentation on dorsum hand and fingers.

benign form of acanthosis nigricans a genodermatosis and suggests that in this type activation of the cutaneous lesions may be produced by the effect of the steroid hormones, whereas in the malignant variety, the tumor or some related substance may be acting in a similar manner.

Case Report.—A. R., a 68-year-old retired naval officer, was first seen in the dermatology out-patient clinic, at Birmingham Veterans Administration Hospital during September, 1947. About 9 months previously he had noticed the appearance of "brown spots" on the backs of his hands. At the same time there was increased dryness and thickness of the skin of the hands, heels and soles. Similar changes occurred in the axillae, groins, intergluteal region and on the ears, corners of the mouth and anterior surface of the neck. There was an associated diffuse hyperpigmentation of the skin, most pronounced in areas normally more deeply pigmented. For the past few weeks before

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admission the patient had noticed progressive weakness, ease of fatigue and lassitude associated with vague digestive complaints and the recent appearance of dark stools. There had been a weight loss of 10 pounds.

Physical Examination. The patient did not appear acutely ill. He was a small, pale, fairly well-nourished well-developed 68-year-old American of English descent whose physical examination was essentially normal except for the presence of the cutaneous lesions. There was a marked dryness and thickening of the skin with accentuation of the normal furrows on the palms, soles and heels. On the dorsa of the hands and wrists there were areas of hyperpigmentation and numerous scattered nodules measuring 2 to 4 mm. in diameter. Similar lesions were present on the external portions of the ears and postauricular regions. In the axillae, both groins and intergluteal area the skin was likewise thickened to form light brown confluent velvety verrucous plaques. The same type of eruption, though less pronounced, was present at the corners of the mouth, on the anterior surface of the neck, the upper part of the chest, and the nipples. Examination of the pharynx was normal, except for a moderate pallor of the mucous membranes.

Laboratory Examination. The significant findings were as follows: hemoglobin 10.5 Gm.; red blood cells 3,400,000; white blood cells 16,050 with a normal differential distribution. There was marked anisocytosis, polychromasia and poikilocytosis of the red cells. Gastric analysis showed no free hydrochloric acid with either the test meal or histamine stimulation.

Histopathologic Examination. A specimen of skin removed from the right axilla showed microscopic features consistent with those found in acanthosis nigricans. There was moderate hyperkeratosis of the stratum corneum and varying degrees of acanthosis of the prickle cell layer associated with a rather marked degree of papillomatosis. The basal cells in most areas showed dense melanin pigmentation, although there was very little pigment evident in the chromatophores in the upper portions of the cutis. The vessels of the papillary cutis were dilated and in some places surrounded by a mild perivascular lymphocytic infiltrate. There was moderate basophilic degeneration of the collagen in the subpapillary cutis. The deeper portions of the cutis showed normal appearing sweat and apocrine glands.

Roentgenologic Examination. Studies of the upper portion of the gastro-intestinal tract revealed a large fungating polypoid mass almost completely filling the upper half of the stomach. At the end of 3 hours there was barium residue retained within the crevices of the mass. Roentgenograms of the chest were normal. Skeletal survey failed to reveal evidence of bony metastasis.

Course in the Hospital. The patient was transferred to the surgical service with the following findings suggestive of gastric cancer: roentgen ray films demonstrating a large mass in the stomach, an achlorhydria, an unexplained anemia and an elevated BMR. Under intratracheal gas-oxygen-ether anesthesia supplemented by small amounts of Pentothal, a trans-gastrectomy was accomplished through the ninth left intercostal space.

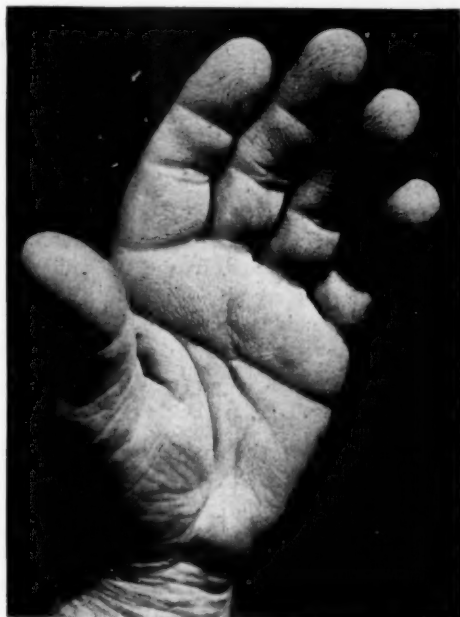


FIG. 3.—This shows marked accentuation of the normal skin markings present on both the palms and soles.

A large tumor, the size of a grapefruit, was found involving the proximal half of the stomach, with gross evidence of metastatic spread of the neoplasm to numerous lymph nodes in the greater and lesser omenta. The excision included the lower end of the esophagus, the greater omentum, gastrohepatic ligament, and all of the stomach except two and one-half inches of the antrum. The antrum was then anastomosed to the esophagus by two rows of interrupted No. 60 cotton and fixed to the under surface of the diaphragm by several interrupted cotton sutures.

On gross examination the excised specimen was a large tumor mass measuring 15 by 8 by 6 cm. growing out of the greater curvature. The surface was fungating, irregular, granular, pink-grey in color, with evidence of superficial hemorrhages. The tumor extended through the serosa to involve the omental attachment on the greater curvature. Along the greater and lesser curvatures there were firm, grayish-white lymph nodes which measured up to 1.5 cm. in diameter.

Microscopically, the tumor was an adenocarcinoma with squamous cell features. There was extension through the gastric serosa and metastasis to lymph nodes in the greater and lesser omenta.

During the first 14 months after operation, the patient gained strength, was able to eat well, maintained a normal hemoglobin and red blood cell count and led a fairly comfortable life for his age. In the fifteenth postoperative month ascites developed, and he died the following month with extensive metastases in the liver, as evidenced on autopsy. The adrenal glands were not involved.

Comment. We were unable to determine in this patient whether the cutaneous manifestations preceded or followed the formation of the tumor. It is quite likely that the two arose simultaneously in view of the nine months duration of the dermatosis and the correspondingly large size of the gastric neoplasm. The patient sought medical advice primarily for the cutaneous lesions and not because of his relative mild systemic complaints. It was only after the diagnosis of acanthosis nigricans was established that our attention was focused on the probability of the presence of a malignant tumor.

In the past, some investigators^{10, 11} have recommended exploratory laparotomy on all patients with acanthosis nigricans. The results, however, have been for the most part disappointing. In a few patients no tumor was found at operation, and yet later, unmistakable signs and symptoms of malignancy appeared. O'Leary¹⁰ cites three instances where early laparotomy without preoperative evidence of tumor failed to reveal any pathologic changes at operation. Two of these patients died later, one with hepatic and the other with gastric malignancy. In the third, no clinical signs or symptoms of neoplasm could be demonstrated five years later. Masson and Montgomery¹¹ describe another patient on whom surgical exploration of the abdominal cavity was performed with negative results, but who died five months later from what apparently was a neoplastic process, although autopsy was not performed. It would therefore appear that this procedure, although logical, has been without much practical benefit. Certainly in the juvenile form it is a method which should be employed only if there is reasonable suspicion of tumor. Probably more basic in management is a thorough clinical, laboratory, and roentgenologic investigation of the patient, with careful follow-up observation at frequent intervals.

SUMMARY

A case of acanthosis nigricans with associated adenocarcinoma of the stomach is reported. A brief review of the essential clinical features of this disorder is given and the possible etiologic factors discussed. The importance of early recognition of this dermatosis by the non-dermatologist is stressed because of its frequent association with malignant neoplasm.

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OVARIAN VEIN PHLEBOTHROMBOSIS AND FATAL PULMONARY EMBOLISM*

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THE SUBJECT OF INTRAVASCULAR CLOTTING is constantly assuming greater importance. Advances are being made to aid deficient blood coagulation, and also to prevent deleterious intravascular coagulation. Too frequently, a technically successful procedure has been complicated by the appearance of pulmonary infarction or fatal embolism. For this reason, interest in venous thrombosis has stimulated investigators to search for the sources of thromboembolic processes, many of which remain obscure. The purpose of this paper is to present an infrequent type of venous thrombosis associated with fatal pulmonary embolism. Although embolism secondary to inflammatory thrombosis of the ovarian veins is not of infrequent occurrence, the incidence of embolism following non-inflammatory thrombosis of these veins appears to be quite rare.

During the month of December, 1948, a case of fatal pulmonary embolism associated with phlebothrombosis of the right ovarian vein was demonstrated at autopsy.† Reviewing our cases, it was found that three months prior to this a previous autopsy had shown phlebothrombosis of the left ovarian vein and a small infarction in the right lower lobe of the lung, without any femoral vein involvement. These cases raised the question as to the incidence of embolism due to ovarian vein phlebothrombosis. The protocols of 319 preceding consecutive hospital autopsies were examined but not one mentioned phlebothrombosis of an ovarian vein.‡ A search of the literature was undertaken, but no previous report was found of fatal pulmonary embolism associated with phlebothrombosis of an ovarian vein.

The diagnostician interested in venous thrombosis knows well that some of the pulmonary complications following surgery, parturition, or severe trauma are due to showers of emboli from thrombosed veins. The incidence of postoperative fatal pulmonary embolism obtained from various authors averages 0.23 per cent (Table I); the incidence of postpartum fatal pulmonary embolism in England reported by Bauer¹ averages one in 2000, or 0.05 per cent; and the incidence of posttraumatic fatal pulmonary embolism seen in 1065 autopsies upon battle casualties was shown by Hamilton and Angevine² to be 66 or 6.19 per cent. Although surgeons and obstetricians direct their attention toward this problem, embolism actually occurs more frequently in the field of internal medicine. Glasser³ has pointed out that 52 per cent of

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‡ Only the last 80 autopsies were performed by Dr. Brill.

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all pulmonary embolism is seen in heart disease; and Hampton⁴ has declared that 30 per cent of all pulmonary emboli and infarctions are derived from non-cardiac medical conditions.

TABLE I.—Incidence of Postoperative Fatal Pulmonary Embolism.

Author Source	Cases of Fatal Embolism	Number of Major Operations	Incidence
Johnson ⁵	6	1,295	0.46%
Henderson ⁶	223	63,247	0.35%
Dougal ⁷	436	161,537	0.27%
Allen, Barker, Hines ⁸	343	172,888	0.20%
*.....	12	6,414	0.19%
Wilson ⁹	47	57,000	0.08%
	1,067	462,381	0.23% average

* St. Mary's Hospital

Statistics obtained from 65,189 autopsies performed during a 25-year period from 1909 to 1934 published by the Weiner Pathological Institute of Vienna¹⁰ show an increase of 1.3 per cent in the recorded occurrence of thrombosis. Whereas some might regard these statistics as indicating a rise in the incidence of thrombosis, we are inclined to believe that a greater number of thrombotic lesions are being discovered because postmortem examinations are being done with greater thoroughness. Current American authors have found that fatal pulmonary embolism is present in about 2.6 per cent of routine autopsies (Table II).

TABLE II.—Incidence of Fatal Pulmonary Embolism in Routine Autopsies.

Author Source	Fatal Embolism	Number of Autopsies	Incidence
Hamilton, Angevine ¹	66	1,065	6.2%
Pilcher ¹¹	130	2,861	4.5%
Graves ¹²	133	3,056	4.3%
St. Mary's Hospital.....	12	319	3.7%
Ochsner ¹³	687	25,771	2.6%
Belt ¹⁴	15	567	2.6%
Collins ¹⁵	891	33,223	2.6%
Collins ¹⁵	227	10,940	2.1%
Cleland ¹⁶	41	3,000	1.4%
	2,202	80,802	2.6% average

Castleman¹⁶ notes that 95 per cent of fatal emboli originate from the deep veins of the leg and the remaining 5 per cent arise chiefly from the heart. The occurrence of leg vein thrombosis found at autopsy is listed by several authors as 81 per cent,² 60 per cent,¹⁴ and 49 per cent.¹⁵ Carlotti¹⁷ describes the presence of thrombosed leg veins in 75 out of a series of 90 autopsies performed after fatal pulmonary embolism. Ochsner and DeBakey¹⁸ believe that "... because of the precipitating factor, circulatory stasis, phlebothrombosis occurs almost without exception in the veins of the lower extremities, where stasis is greatest." However, Beck¹⁹ has said "... a fair percentage of (venous) emboli arise from sources other than the veins of the legs." The pathologist must carefully search for all sources of emboli, for some are easily missed. In the absence of demonstrable involvement of leg veins, what other

venous systems may be the source of embolism? McPheeters²⁰ has stated ". . . I believe there is a phlebothrombosis of the pelvic and hypogastric veins far more often than we think."

DeTakats²¹ has noted that venous stasis in the pelvic area is favored by tortuous sinuses of the hypogastric veins and the hypostatic obstacle of the high sacral concavity which becomes pronounced when the patient is supine. He feels that the proximity of the pelvic veins to organs which may become chronically infected, such as the bladder, uterus, rectum, and prostate, predisposes to the formation of thromboses, and he²² points out that the surgeon often sees plugged veins in the broad ligament when it is transected during hysterectomy. Koehler²³ has observed that 80 per cent of the roentgen ray plates of the adult pelvic region demonstrate one or more phleboliths.

TABLE III.—*Sites of Venous Thromboses Found at Routine Autopsy.*

Veins Involved		Total Involve- ment	Incidence Specific Vein Involvement
Left ilio—femoral.....	24)28 29)48 19)27 99)116 33 21 273 50.5%		
Right ilio—femoral.....	4)28 19)48 43 47 17 .. 107 19.8%		
Heart..... 12 .. 44 2 67 12.4%		
Periprostatic.....	2 7 1 9 24 .. 1 35 6.5%		
Hypogastric..... 2 7 1.3%		
Portal.....	5 2 7 1.3%		
Hemorrhoidal.....	3 3 1 7 1.3%		
Vena cava.....	2 3 1 6 1.1%		
Basilic.....	2 2 1 6 1.1%		
Vesicle..... 5 .. 5 0.9%		
Mesenteric.....	4 4 0.7%		
Ovarian.....	2 1 .. 3 0.6%		
Left jugular.....	3 3 0.6%		
Pulmonary.....	3 3 0.6%		
Sagittal sinus.....	2 1 .. 3 0.6%		
Sigmoidal.....	2 2 0.4%		
Splenic.....	2 2 0.4%		
Spermatic.....	.. 1 1 .. 2 0.4%		
Renal.....	.. 1 1 2 0.4%		
Appendiceal.....	1 1 0.2%		
Site of herniorrhaphy..... 1 1 0.2%		
Number thromboses found.....	61 65 94 187 106 26 539*		100%
Number autopsies.....	780 3,672 247 10,940 635 246 16,520		

Author source: McNamara²⁶, Zahn²⁷, Westdahl²⁸, Collins¹⁸, Moran²⁵, Ingraham²⁹

* Many sources of embolism were undetermined.

One of the editors of the section on "Queries and Minor Notes" of the Journal of the American Medical Association²⁴ replied to a question on thrombosis of the left ovarian vein as follows: Ovarian vein thrombosis is occasionally seen during operation and is usually limited to one ovarian vein; rarely both ovarian veins are affected; when the patient is questioned following operation, no history can be obtained of unusual symptoms related to the thrombosis; evidently there seem to be no pathognomonic signs or symptoms accompanying involvement of the ovarian veins; likewise, there seem to be no sequelae after the discovery of thrombosis in an ovarian vein at time of operation.

Table III tabulates the various sites of venous thrombosis found by several authors in their routine autopsies. Moran²⁵ mentions only one, and McNa-

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mar²⁰ only two, cases of intravascular clotting involving the ovarian veins. The compiled statistics show that a total of 16,520 routine autopsies demonstrated thromboses in 539 instances. The incidence of ilio-femoral thrombosis was 50.5 per cent, hypogastric thrombosis was 6.5 per cent, and ovarian thrombosis was 0.6 per cent. The statistics in these cases made no attempt to differentiate between phlebothrombosis and thrombophlebitis.

Herrmann³⁰ has indicated that varying degrees of thrombophlebitis of the ovarian and hypogastric veins usually follow a suppurative process in and around the uterus, due most frequently to puerperal sepsis or pelvic peritonitis secondary to septic abortions. Ochsner¹³ states that the septic type of thrombophlebitis is dangerous because of the production of ferments, associated with the thrombophlebitic process, which liquefy the clot and hence permit detachment and septic embolism. In 100 cases of puerperal pyemia reported by Miller,³¹ there was involvement localized to one of the ovarian veins 75 times, and to both ovarian veins five times, to one hypogastric and one ovarian vein six times, and to one common iliac vein eight times. Collins and Nelson³²

TABLE IV.—Incidence of Pelvic Vein Thrombosis Seen at 14 Operations.

Type of Thrombosis	Accompanying Pathology	Number Cases	Number of Times Each Specific Vein Was Involved				
			Ovarian	Uterine	Hypogastric	Iliac	Caval
Phlebothrombosis	"Fibroids"	2				2	
Thrombophlebitis	Postabortion sepsis	5	4	3	1	1	1
	Postpartum infections	6	5	2	1	2	
	"Hysterectomy"	1		1			

report that during a period of nine years at the Charity Hospital in New Orleans, there were 536 deaths of 32,198 patients admitted to the Gynecological Service. Of those who came to autopsy, 50, representing 9.3 per cent, showed antemortem pelvic vein thrombosis. In 12 cases the clotting was described as phlebothrombosis and in 38 cases it was described as thrombophlebitis; only in this latter group did fatal pulmonary embolism occur. To prevent this catastrophic complication, Ochsner¹³ believes that early ligation of the vena cava just above its origin, and ligation of both ovarian veins, will prevent septic infarcts and pulmonary gangrene; and that such a procedure may be life-saving if performed before embolism has occurred. High saddle thrombosis may be treated by vena caval ligation. Glasser³ has followed five cases of caval ligation for one year, and not one died or showed postoperative edema. Allen³³ offers information on ten additional cases of vena caval ligation for iliac thrombophlebitis; these demonstrated a rapid subsidence of the inflammatory process and a few developed minimal postoperative edema.

Two cases of phlebothrombosis and 12 cases of thrombophlebitis seen at operation have been presented by Collins and Nelson;³² they indicated the incidence of specific pelvic vein thrombosis encountered in their series (Table IV). It is interesting that the ovarian veins were uninvolved in either case of phlebothrombosis, while they were involved in all but one of the cases of thrombophlebitis. Symptoms and signs differentiating pelvic vein phlebo-

thrombosis and thrombophlebitis, as found by these authors, are represented in Table V. No case of phlebothrombosis was accompanied by chill or pulmonary infarction, fever was only mild, and edema was present in all cases; whereas, all cases of thrombophlebitis was accompanied by chill, all but one was accompanied by pulmonary infarction, fever was high (103-106), and edema was present in only some of the cases.

Although the clinical impression can be grossly incorrect, involvement of the pelvic veins by thrombosis according to various authors can give rise to: edema of the genitalia,³⁴ of the suprapubic region,²¹ of the buttocks and adductor muscle region, close to the inguinal folds,³⁵ and of the abdominal wall superior to the inguinal level;³⁴ recurrent pain of sciatic and femoral distribution resembling causalgia;³⁵ pain in the region of the buttocks or adductor

TABLE V.—*Differentiating Points Between Pelvic Vein Phlebothrombosis and Thrombophlebitis.*

Type of Thrombosis	Number Cases	Chill	Fever	Pulmonary Infarcts
Phlebothrombosis	2	none	mild	none
Thrombophlebitis	12	all	103-106	all but one

muscles close to the inguinal folds;³⁰ frequency of urination;³⁰ occasional slight diarrhea;³⁰ and apprehension.¹² Cords may be palpated on pelvic examination at the site of the large veins of the pelvis lateral to the uterus.³⁰

CASE REPORT

* F. M., a 72-year-old white female, was brought to the hospital by ambulance and admitted* per stretcher on December 13, 1948. She was a known diabetic, controlled by diet. For several months prior to admission the patient had steadily lost weight and strength. Her brother noticed that during these months she would not exercise or perform muscular activity any more than was absolutely necessary. She became nervous, highly excitable, and frequently talked to herself. Two months before admission relatives observed that her skin developed a greyish, ashen color which persisted for about 3 days. Shortly after this she slipped and fell, bruising her right hip. Following the accident she began to cough repeatedly, and the week before admission she exhibited minor episodes of hemoptysis.

Physical examination on admission revealed an obese, dyspneic, rather drowsy white female whose answers to questions were incoherent. She had an increased pulse and respiratory rate but her temperature was normal. Her blood pressure was 150/90; there was a soft, blowing, distant murmur, heard best at the apex and not transmitted; heart sounds were of good tonal quality and the rhythm was regular; generalized crackling râles were heard over both lung fields; and there was pitting edema of the legs, abdomen and back.

The urine on admission showed a four plus albumin; it contained some granular casts and a few red and white cells per high power field. Repeated urine tests showed no change. The blood count probably represented a condition of anhydremia, for there were 5 million red cells, 120 per cent hemoglobin, and 14,500 white cells, with a differential of 46 polymorphonuclears and 33 per cent stab forms. After 3 days of therapy, the red cell count dropped to 4 million and there was 92 per cent hemoglobin. A later white count revealed 4000 cells with a differential of 47 per cent polymorphonuclears, 2 per cent stab forms, and 51 per cent lymphocytes. The Kahn was negative and the admission

* Service of Dr. J. J. Maloney.

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blood sugar was 245 mg. per 100 cc. Subsequent blood sugar levels were slightly above normal.

After the first 3 days of treatment, the patient lost considerable edema fluid and her answers to questions were coherent and she was co-operative and cheerful. On the fifth hospital day she began to experience mid-abdominal pain; the pain became more severe and for the next three days she groaned continuously. On the twelfth day she was quiet but restless, and the following day she expired.

The temperature, pulse and respirations reached normal limits 2 days after admission and remained so until the ninth hospital day when a definite spiking occurred in the values of all three. At that time no satisfactory explanation could be found. Thereafter, the T.P.R. values fluctuated until the patient expired 3 days later.

Gross findings at autopsy revealed moderate *cardiac* hypertrophy, slight narrowing of the coronary vessels, and no thrombi in the auricular appendages. Each *pleural* cavity contained 20 cc. of a brownish turbid fluid. The *diaphragm* rose to the third intercostal space on the right and to the fifth space on the left. A large branch of the right *pulmonary artery* (Fig. 1) was completely occluded by an antemortem thrombus measuring from 0.5 to 0.9 cm. in diameter. There were two wedge-shaped infarcts present in the right lower lobe and one infarct in the left lower lobe of the *lung*. The *trachea* and bronchi contained a moderate amount of muco-hemorrhagic frothy fluid. The *uterus* (Fig. 2) was enlarged, nodulae (due to the presence of leiomyomata), and congested; on cut section, organized thrombi were seen in the vessels of the myometrium. The *right adnexa* was firmly adherent to the right posterior aspect of the uterus and to the adjacent sigmoid colon. The right ovarian plexus contained many dilated, tortuous, and thrombosed veins. The right *ovarian vein* (Fig. 3) was completely thrombosed and measured over one and a half centimeters in its largest diameter. The *femoral veins* milked freely.

The significant microscopic findings were passive congestion of the liver and spleen, arteriolarsclerosis of the kidneys and adrenals, leiomyomata of the uterus, pulmonary infarcts, and, phlebothrombosis of the right ovarian vein.

Sections from the infarcted pulmonary areas showed the presence of not-yet organized arterial emboli, and also, older emboli that were completely organized and recanalized.

Sections through the thrombosed right ovarian vein showed no active inflammatory changes present in the wall of the vein. A peripheral portion of the thrombus demonstrated organization by fibroblasts and newly formed capillaries. The major part of the thrombus, however, was formed by successive layers of red cells, fibrin, and leukocytes.

CONCLUSION

The episodes of hemoptysis and cyanosis witnessed at home prior to the admission of the patient, as well as the severe dyspnea and development of

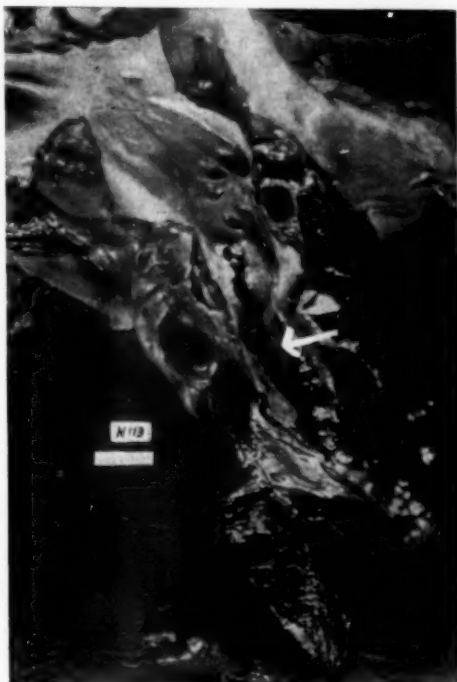


FIG. 1.—Embolus in large branch of right pulmonary artery.

abdominal pain³⁶ observed during her stay in the hospital, may well represent the effects of recurrent embolic showers.

Ochsner defines phlebothrombosis as "an intravenous clot unassociated with an inflammatory process in the venous wall."³⁷ Therefore, since this case presented no microscopic evidence of an inflammatory process of the vein wall, it can be concluded that the intravascular clotting demonstrated in the right ovarian vein was one of phlebothrombosis.



FIG. 2

FIG. 2.—Mid-sagittal section of uterus showing fibroid and dilated thrombosed veins.

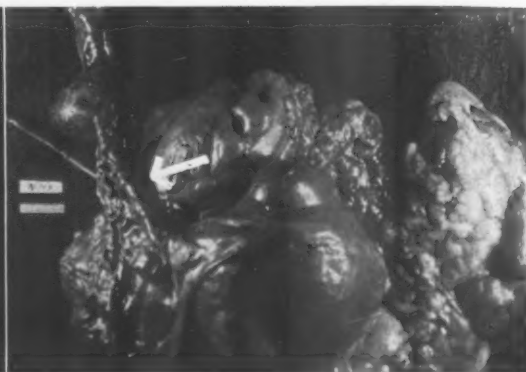


FIG. 3

FIG. 3.—Enlarged, distorted uterus with thrombosed, dilated right ovarian vein.

It is possible that the phlebothrombosis readily demonstrated in the right ovarian vein could have caused the fatal pulmonary embolism.

However, it is also recognized that the evidence presented does not establish the source of the fatal embolus as having originated from the thrombosed right ovarian vein, for although the femoral veins milked freely at autopsy, a complete leg dissection was not performed, and, there immediately arises the debatable issue whether or not a thrombotic process could have been present in the leg veins that might have given rise to the fatal embolus.

SUMMARY

1. Although embolism secondary to inflammatory thrombosis of the ovarian veins is not of infrequent occurrence, the incidence of embolism following non-inflammatory thromboses of these veins appears to be quite rare.
2. A case of phlebothrombosis of an ovarian vein associated with fatal pulmonary embolism is presented.

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SURGICAL THERAPY OF DECUBITUS ULCERS IN THE PARAPLEGIC PATIENT*

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FEW STUDIES ARE AVAILABLE to stress the importance of the decubitus ulcer and its medical and surgical management. Pessimism still permeates the minds of the profession when the ultimate fate of the paraplegic patient is considered. The decubitus ulcer in the paraplegic is a visual announcement of the patient's fate, unless the attending physicians realize that the ulcer or ulcers *per se* are not death-dealing and must not be accepted as such. Therapeutic vigor appears to parallel the physician's information and enthusiasm to overcome the hazards of the ulcer.

It is our intention to report briefly our experiences with these ulcers in the hope that another recording of successful results will help to erase the pessimism about the subject.

In 1938, Davis reported the excision of scars of decubitus ulcers; the denuded area was then covered by a flap of skin and underlying adipose tissue.⁷ Lamon and Alexander,¹⁰ in 1944, excised and closed in linear fashion three small decubitus ulcers with good results. After this, other reports of fairly large series of cases began to appear in the literature. These earlier reports in the main described the closure of ulcers by various plastic procedures involving skin only, although Conway, *et al.*⁴ mention the need for the resection of fragmented or necrosed bone underlying the ulcer. In 1947, Kostrubala and Greely⁹ recommended, after excision of the ulcer, the radical removal of the underlying bony prominences along with the shifting of adequate skin flaps. This, it seems to us, has been a real step forward in the permanent eradication of ulcers, for, as these authors point out, osteotomy removes the underlying bony pressure point and also takes away abnormal or diseased bone. This technic has been routinely used where applicable in the treatment of all ulcers reported in this series.

This report is based on experience derived from the 250 bed Paraplegia Service of the Kennedy Veterans Administration Hospital. During the period from September 1, 1947, to July 15, 1949, the surgical attack on the pressure sore at this institution has been executed almost exclusively by one or the other of the co-authors. Only those procedures personally performed by them are herein considered. During this period, 175 operations have been performed on 153 decubitus ulcers in 123 patients.

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The hospital was visited in October, 1947, by Dr. Joseph Kostrubala,* and gratitude is expressed to him for many of the ideas used in the surgical repair of these lesions, most notable of which is the radical ischial ostectomy in the treatment of the ischial decubitus.

INCIDENCE

The total incidence reported in the literature varies from 57 to 85 per cent of paraplegic veterans of World War II.² The majority of our new cases have been referred to us after an early short stay in civilian hospitals; the ulcer incidence rate is extremely high. Conway and co-workers⁴ report the incidence with regard to location as follows:

Sacral.....	21%	Knees.....	8%
Trochanteric.....	19%	Ant.-sup. iliac spine.....	6%
Heels.....	19%	Pretibial.....	4%
Ischial.....	10%	Elsewhere.....	13%

In April, 1949, 24.3 per cent of the total number of paraplegic patients at Kennedy Veterans Administration Hospital had ulcers. In regard to location, their incidence was as follows:

Sacral.....	41%	Ischial.....	22%
Trochanteric.....	25%	Elsewhere.....	12%

From these figures it can be seen that the ulcers about the pelvic girdle have become the important ones, a fact previously recognized.⁹ This situation exists in spite of the fact that our surgical campaign has been directed most vigorously against these particular ulcers.

SPONTANEOUS HEALING

Before discussing the surgery of bedsores it must be emphasized, however, that surgical repair is not indicated for all ulcers. Many, perhaps most, will heal spontaneously with improvement in the nutrition of the patient.

Spontaneous healing depends upon the extensiveness of the anesthetic area, the site of the anesthesia, the maintenance of proper nutrition, the necessary abortive measures, such as turning, Stryker frame, etc., the warding off of a series of repeated infections notably occurring in the genito-urinary tract with subsequent debilitating states, the co-operation of the patient and the alertness and energy of those who are responsible for the patient's care. Perhaps this spontaneity of healing is best delegated to prophylactic measures in regard to the formation of the ulcers. Actually, it should be regarded as the most important phase, and therefore the need for surgery exists when these other measures have failed.

During the period from March, 1947, to January, 1948, approximately 100 ulcers were repaired surgically, and in this same period of time approximately another 100 ulcers healed spontaneously. This was accomplished in spite of the fact that more than 100 patients were discharged during this period and new admissions over the same period almost invariably had a

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large number of serious-type ulcers. It is, of course, true that spontaneous healing is accomplished by granulation and subsequent scar formation. This avascular scar is quite prone to repeated ulceration, particularly when it overlies a bony prominence.

Surgical repair, then, is indicated on those ulcers which will not heal by medical measures or, having healed by scar tissue, are of such location and magnitude that repeated breakdowns either occur or can be predicted with reasonable certainty.

THE ISCHIAL ULCER

Of the several ulcers, from the standpoint of anatomic location that most frequently demand surgical repair, the ischial ulcer is by far the most important. It is the ischial area that must bear the brunt of the paraplegic individual's weight as he leaves his bed for the wheel chair. Frequently, his ability to become rehabilitated to a gainful occupation or to maximum social independence is seriously challenged by his inability to maintain well-healed buttocks. If a healed scar is present in this area it is obvious that scar tissue with its relative avascularity cannot hold up in the face of pressure from a bony prominence. Therefore, whether an ischial ulcer heals spontaneously or not, experience has led us to believe that surgical repair is always indicated to prevent serious recurrent ulcerations with attendant infection. For these reasons most of the surgical attack on the decubitus problem at this institution has been directed at the ischial decubitus.

PREOPERATIVE AND POSTOPERATIVE TREATMENT

When the ulcer patient is in a good state of nutrition and his ulcer is clean, he is ready for operation. The subject of nutrition in preparing paraplegic patients for surgery has been well covered in the literature^{3, 4, 6, 8} and will not be elaborated here. In general, if the patient is eating well and gaining weight, he is considered ready for operation.⁴ Locally, when the ulcer shows clean, healthy granulations and is without necrotic tissue, surrounding cellulitis, or pockets of pus, it can safely be surgically repaired. This state can usually be attained by mechanical debridement, wet dressings (usually of saline or dilute acetic acid), one of the bland ointments, or a combination of these measures. In some cases that have cleaned up slowly or poorly on this regimen, wound excision and osteotomy have been carried out, leaving the wound open. This procedure has been most successful in getting quickly a clean granulating wound for subsequent plastic closure.

Many patients in this series have had spasms of skeletal muscle. Mild or moderate spasms have been no deterrent to ulcer surgery; a few patients, however, have had such severe spasms as to put in jeopardy any plastic operative procedure. This problem in these individuals has been well handled by the neurosurgical service by appropriate rhizotomy, thus making possible subsequent ulcer closure and in a few of our patients has been a *sine qua non* to insure successful ulcer surgery.

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On the day before operation, all patients are started on penicillin, and if they can tolerate sulfonamides these drugs are started also. One of us (E. S. M.) used routinely one of the intestinal sulfonamides (usually sulfa-guanidine), the other (C. L. C.) did not; as far as can be observed there has

FIG. 1



FIG. 2

FIG. 1.—Preoperative view of a typical bilateral ischial decubitus ulcer. Note the bony overgrowth, scarred edges and depth of ulceration.

FIG. 2.—The postoperative status of the same patient as shown in Figure 1, six months following repair. A pedicle graft combined with split thickness graft was used on the left side and a pedicle graft alone was used on the right. The split thickness graft is to one side of the weight bearing area.

been no difference in results attributable to these drugs and it is now felt that they are unnecessary.

Postoperatively, the patient is placed on a Stryker frame. He is turned so that his weight is off the operative site three-fourths of the time. A retention catheter is placed in the bladder routinely before operation. A low

residue diet is given, and on the seventh postoperative day a bowel movement is encouraged with the aid of an enema. In some cases, constipating drugs have been used, but in general this has not been necessary. Sometimes when a patient complains of distention and discomfort he is given an enema on the fifth or sixth postoperative day without, thus far, any injury to his wound. Most patients run a low grade fever for a few days after operation. Usually sulfonamides are kept up until the temperature has been normal for 24 hours, and penicillin is continued for 24 hours more. "Ambulation" by wheel chair is allowed in about three weeks (assuming primary healing) or longer if necessary until solid healing has taken place.

It must be recognized by both physician and patient that these operations, curative in most instances, do not guarantee against recurrence. In order to obtain a lasting good result, it is essential that the patient remember that he may get pressure sores as long as he is without feeling and that he must exercise eternal vigilance to guard against this eventuality. Late recurrences consequently will appear in the patient who is not intelligent or not willing to expend thought, alertness and energy to prevent the reappearance of the ulcer as long as the anesthesia persists.

TECHNIC

The general principles of surgical treatment are briefly enumerated: (1) The ulcer and surrounding scar are completely excised; (2) the underlying bony prominence is as radically removed as is consistent with function; (3) wherever possible, a pad of muscle or fascia is provided to cover the bone; (4) the skin is closed without tension over the defect by pedicle graft alone, pedicle graft and split thickness graft, or when possible by simple closure. Ideally, this provides a full thickness of skin and fat at the original ulcer site. In cases where the above principles cannot be observed because of poor condition of the patient, or because of an insufficiency of adjacent unscarred skin, a split thickness graft may be more expedient even if used only as a temporary measure to stop protein loss. Obviously a split thickness graft over the area of the ischial tuberosity would be unsatisfactory as a permanent repair.

As has been indicated, the ulcers about the pelvic girdle are the ones most often requiring surgery. They fall into three principal groups, the trochanteric, the sacral and the ischial.

The Repair of the Ischial Decubitus. The ulcer and surrounding scarified area are excised in toto. The ischial tuberosity, the superior and inferior ischial rami and most of the inferior pubic ramus are resected. A pedicle graft is outlined from the adjacent thigh or buttock. Usually this pedicle is from the lateral and inferior border of the defect with its base directed inferiorly and medially. This maneuver makes the biceps femoris muscle easily available. Frequently the defect left by osteotomy is filled by cutting the biceps femoris muscle four or five inches below its origin, reflecting it upward, and suturing it to the obturator internus and the gluteus maximus muscles. Sometimes the gluteus maximus muscle alone can be used to fill the defect. By either method a rounded contour for the buttock should be obtained with absolutely no dead

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space. Catgut is used for buried suture. The pedicle graft is rotated to cover the original site of the ulcer. This should be done with the patient flexed on the table almost to 90 degrees so that no tension will be on the suture line

FIG. 3



FIG. 4

FIG. 3.—A preoperative roentgenogram of the same patient seen in Figures 1 and 2, showing size of the ischial tuberosities.

FIG. 4.—This film shows the extent of the osteotomy. On the right the ischial rami, ischial tuberosity and inferior pubic ramus have been removed. Some regeneration has occurred on the left.

when the sitting position is resumed. Usually a split thickness graft is necessary to cover the donor site of the pedicle graft. In our series, split thick-

ness grafts used at the donor site of the pedicle graft have rarely broken down, and it is felt that avoidance of tension is more important than avoidance of split thickness graft. Frequently in smaller ulcers or in ulcers that have healed by scar, simple closure may be employed without tension if the osteotomy has been sufficiently radical.

The sacral decubitus ulcer is treated by excision of the ulcer and scar, the leveling of any small bony projection of the outer sacral table, and rotation of a large pedicle graft. This graft is designed to be sufficiently large to avoid



FIG. 5.—An example of simple closure following excision of a small ulcer. Photograph was taken nine days postoperatively. Two weeks postoperatively, the closure was solid.

a suture line being left over the sacrum. It is usually rotated from the lumbar region downward. Occasionally in debilitated patients or in patients who have no unscarred adjacent skin, a split thickness graft is applied to the granulating base over the sacrum.

The trochanteric ulcers are treated by excision of the ulcer, the surrounding scar tissue and the entire greater trochanter. Usually the bone can be covered with a layer of adjacent fascia or muscle before covering with a pedicle flap, but occasionally a flap of skin and fat has been applied directly over the bone and a good result obtained.

ANALYSIS OF RESULTS

A total of 175 operative procedures have been performed on 153 ulcers occurring in 123 patients. One death occurred early in the series, giving an operative mortality of 0.6 per cent.

The immediate results are shown in Table I. We have arbitrarily classified the results as good, satisfactory and poor. A good result is one in which the pedicle heals per primam and a sufficiently high percentage of the split graft takes so that the wound is completely healed in two to three weeks. A satisfactory result is one in which complete healing is obtained in four to

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five weeks, the delay being caused by hematoma, mild drainage from the suture line, or loss of a considerable portion of the split thickness graft. A poor result is one where the ulcer fails to heal in five weeks, or heals sooner but produces so much scarring that the repair is unstable.

TABLE I.—*Immediate Results.*

Location of Ulcer	Number of Cases on Which Repair Attempted by Any Method	Satisfactory Results		
		Good Results		Poor Results
Ischial.....	82	53	26	3
Trochanteric.....	35	16	14	5
Sacral.....	28	21	4	3
Miscellaneous.....	8	5	1	2
Total.....	153	95	45	13
Percentage.....	100	62	29	9

There were 95, or 62 per cent, classified as good, 45, or 29 per cent, satisfactory, and 13 cases, or 9 per cent, as poor. Therefore, surgical repair might be said to have been successful in 91 per cent of the cases and unsuccessful in 9 per cent.

Eighty-seven of the cases classified as good or satisfactory have been followed two to seven months for an average of three months. The number and percentage of breakdowns are shown in Table II.

TABLE II.—*Short Term Follow-Up.*

Location	Number of Cases	Breakdowns	Percentage of Breakdowns
Ischial.....	56	2	4%
Trochanteric.....	20	3	15%
Sacral.....	11	2	18%
Total.....	87	7	8%

Many of our cases have been operated upon in the last year; many others have been lost through transfer or discharge: However, 14 of the early successful ischial repairs were re-examined 18 to 21 months postoperatively. Ten were in good condition, two had developed frank recurrences, one had developed a deep sinus lateral to the repair and one had developed a superficial ulceration. One of the cases which had remained well healed is shown in Figure 2. Five large pedicle graft repairs of sacral ulcers were followed 18 months or longer and all were in good condition. Three split thickness grafts over the sacrum were followed the same length of time and two showed small recurrent ulcerations. Of six trochanteric ulcers treated by pedicle flap, one showed a recurrence after 18 months.

COMPLICATIONS

There has been one postoperative death in the series. This occurred on the third postoperative day following the repair of a moderate-sized sacral

ulcer and was attributed to delayed vascular collapse. Systemic complications have been few. There was one case of phlebothrombosis, one case of epididymitis, and one severe urinary tract infection (which might have occurred without surgery). A few patients showed fairly mild effects of sulfonamide or penicillin hypersensitivity which cleared up promptly when the offending drug was discontinued.

Most of the wounds healed per primam, a fact that is rather astonishing in view of the varied and abundant surface contamination. Major wound infections have been a rarity, but a number of minor wound infections have occurred. In the main these have done little except to retard healing for a week or so. A few cases developed collections of serum which disappeared after aspiration and the application of pressure dressings. In five cases there was minor postoperative hemorrhage, usually controlled by packing or pressure dressings. Some few wounds have separated after removal of the skin sutures and have required secondary suture; two of these were in patients who left the hospital AWOL within a few days after operation. In some cases there has been the loss of part of a flap, or part or all of a free graft; these wounds have often healed without further surgery.

SUMMARY

A series of 175 operative procedures performed on 153 ulcers occurring in 123 patients has been presented. Ulcer incidence, pre- and postoperative treatment, and operative technic have been discussed.

Immediate, short term, and long term results have been listed and the commoner operative complications have been mentioned.

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Editorial . . .

THE RESPONSIBILITY OF HOSPITALS AND THEIR SURGICAL STAFFS TO RESIDENTS

THE DIFFICULTIES that many hospitals encounter in obtaining a sufficient number of residents is being reflected in requests for recognition by the various certifying bodies as suitable for postgraduate training. The smaller hospitals in particular are confronted with a perplexing problem. A desire to help these hospitals and their staffs to solve their troubles should not be allowed to influence unduly those responsible for the grading of hospitals. The surgical staffs of hospitals should realize that in undertaking to train surgeons they assume a real responsibility. The material requirements, an adequate number of public ward beds, proper laboratory space and equipment, etc., are relatively easy to assess and are important. They will not of themselves, however, train surgeons. The surgical staff must be composed of men who are capable of teaching not only the practical aspect of surgery, but something of the related basic sciences. In addition, they must be men anxious to teach and sufficiently unselfish to be willing to devote many hours of their time to the training program, even though this involves a financial sacrifice. It is much more trying and time consuming to assist a less experienced man from the other side of the table than to do the operation oneself. Nonetheless, this apparent waste of time must be accepted if one has assumed responsibility for the teaching of surgeons. In actual fact, this apparent self-sacrifice carries its own reward in that the rapid increase in the capabilities of the resident makes it possible to throw a greater share of the responsibility upon him.

The requirements that have been laid down as necessary for admission to the examinations for higher degrees in the United States and Canada demand that a young man spend five or six years in postgraduate training. It is unfair that he should be asked to spend any part of that time, usually with little if any remuneration, merely as a servant of a hospital. The practice of allowing superintendents of hospitals to choose trainees should be frowned upon. Only promising applicants should be accepted, and the choosing of them should be the responsibility of the surgical staff. It is not a kindness to permit a young man who is unlikely to pass the examinations at the end of his training to embark upon or to continue years of preparation. Higher degrees are likely to be demanded as a requisite for a hospital appointment in the near future and those who have been unable to obtain them will not be permitted to do surgery. Entrants should, therefore, be chosen with care, and once chosen given every opportunity. Those who fail to show satisfactory progress either because of inaptitude or lack of application should be weeded out.

The part that private clinics may be permitted to play in a training program is difficult and controversial. There is no doubt that experience gained by merely assisting with operations cannot be compared with that obtained

in a public general hospital, where residents have a gradually increasing responsibility thrust upon them and are permitted actually to assume responsibility for patients and to perform operations of ever-increasing magnitude. Valuable experience of a somewhat different kind from that obtainable in a general hospital can, however, be received in clinics. Some combination of the two types of training should be acceptable.

It has been assumed thus far that places can be found for as many men as can be trained in the specialties. This may remain true for a few more years, but the saturation point is within sight. It is doubtful if it is necessary to continue to expand the facilities for training. It will be much better to emphasize quality rather than quantity.

It may be that the problem of the hospitals not equipped to train surgeons can be solved by including them in a program of training of general practitioners. This is just as important as the training of surgeons, but the requirements are somewhat different. Some recognition of such training could be allowed in the case of those who change their minds, or after a time, in practice decide to embark upon a course of specialist training.

ROBERT M. JANES.

BOOKS RECEIVED FOR REVIEW

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| LUCK, J. VERNON | <i>Bone and Joint Diseases.</i> Charles C. Thomas, Springfield, Illinois, 1950. (589 pages; \$16.50) |
| STEINDLER, ARTHUR | <i>Post-graduate Lectures on Orthopedic Diagnosis and Indications.</i> Volume I. Charles C. Thomas, Springfield, Illinois, 1950. (278 pages, \$7.50) |
| BAILEY, HAMILTON | <i>Pye's Surgical Handicraft.</i> The Williams and Wilkins Company, Baltimore, Maryland, 1950. (702 pages; \$6.00) |
| MAJOR-GENERAL SIR HENRY
LETHEBY TIDY, Honorary Editor | <i>Inter-allied Conferences on War Medicine.</i> Staples Press Limited, New York, New York, 1947. (524 pages; \$5.00) |
| TITUS PAUL | <i>The Management of Obstetric Difficulties.</i> The C. V. Mosby Company, St. Louis, Missouri, 1950. (1016 pages; \$14.00) |
| POHL, JOHN F. | <i>Cerebral Palsy.</i> Bruce Publishing Company, Saint Paul, Minnesota, 1950. (213 pages) |
| SANER, F. D. | <i>The Breast. Structure-Function-Disease.</i> The Williams and Wilkins Company, 1950. (308 pages; \$8.50) |

BOOK REVIEW

PROCEEDINGS OF THE FIRST CLINICAL ACTH CONFERENCE. John R. Mote, M.D., Editor, The Blakiston Co., Philadelphia, 1950.

On October 21 and 22, 1949, a meeting was arranged in Chicago under the sponsorship of Armour and Company. This was planned by Dr. John Mote, the medical director, to bring together the many investigators who had been working throughout the country with ACTH. ACTH (adrenocorticotrophic hormone) is the active principle prepared from anterior pituitary of the hog which produces widespread effects by stimulation of the adrenal cortex and release of adrenal hormones. This hormone had been fractionated and purified by Armour and Company and was first made available for study in 1946. In the three years which followed, much work had been done and it was the purpose of the meeting to review this work. Each speaker presented a brief summary of his work. These summaries were transcribed to make a monograph of the meeting which was to be circulated privately to those who attended. It soon became obvious that the proceedings were of such exceptional interest that they should be made available to the general medical public. For this reason, the proceedings of the meeting were brought together in a book which has now been published under the above title.

To this reviewer there seem to be three general observations which have emerged from this work, of which every surgeon should be aware. These three broad categories are as follows:

1. Surgical operations produce a secretion of ACTH from the pituitary which in turn stimulates the adrenal cortex to release its steroid hormones. This increased secretion of circulating adrenal cortical hormones produces many peripheral effects, amongst which is a lowering of the total blood eosinophile count. The eosinophile count, therefore, provides us with a readily measurable clinical test of the activity of this pituitary-adrenal axis in response to injury or stress.

2. A wide variety of conditions are affected profoundly by the administration of ACTH. It is beyond the scope of present knowledge to explain the common denominators in these multitudinous conditions. There are certain clues to suggest that adrenal cortical stimulation by ACTH produces some alteration in the mesenchymal structures of the body with a decrease in fibrous tissue growth and a diminution in the intensity of immune or hypersensitivity responses with a shift in chemical balance characterized by a loss of potassium and a tendency to retain sodium. The wide variety of disease states improved by this therapy are of tangential interest to surgery because of the fact that patients suffering from such diseases may have to be operated upon. In certain instances pre-treatment with ACTH may convert the patient into a better candidate for operation. This may apply to arthritis, rheumatic conditions of the heart, hemolytic processes, certain types of nephritis, ulcerative colitis and a miscellany of other conditions, pituitary tumors, and myxedema.

3. Of more especial interest to surgeons is the fact that the metabolic response to a dose of ACTH resembles in many of its general features and several of its particular details the metabolic response elicited by a surgical operation. The administration of 40 mg. of ACTH appears to produce an operative response in miniature. This should guide us to a more adequate understanding of the reaction of the human organism to injury and the role of that response in repair, recovery and convalescence.

Turning now to the book itself, no effort will be made to review all 52 of the articles because of their scope and detail. Only those which appear to be of particular interest to the surgeon will be touched upon briefly. In the ensuing review, for purposes of brevity, the last name of the author and the number of the paper will be indicated to identify each section mentioned.

Randolph (1) discusses eosinophile counting technics. This paper and the subsequent discussion by other workers should be consulted by any one wishing to use the

eosinophile count in conjunction with the care of surgical patients. The method of Randolph, while somewhat more cumbersome than the eosin-acetone method, has the advantage that the blood can be kept in a pipette for several hours without a change in count. By the simpler method (with eosin and acetone) the blood must be counted immediately after dilution. In general, a laboratory doing only occasional eosinophile counts is well advised to use the method of Randolph, whereas one carrying out the counts routinely in large numbers of cases can satisfactorily adopt the method of eosin and acetone used by Thorn and his group.

The article of McIntosh (2) describes the metabolic changes produced by the injection of ACTH in normal individuals. The book as a whole is a mine of metabolic information; this article outlines the ground rules by demonstrating the characteristic changes. These consist essentially of the retention of sodium and water, the loss of potassium, sulfate and phosphate and a small loss of nitrogen with the excretion of the urinary end-products of steroid hormones. It is important to emphasize that the metabolic changes produced by the injection of ACTH vary between individuals and vary in the same individual in successive experiments. One may occasionally observe a situation in which the metabolic effects are almost exactly the reverse of the "classical" changes.

Solomon (5) shows that elderly people respond normally to ACTH. This is important in relation to the metabolic changes produced by surgery: in most instances age alone does not alter the response. Age plus debility reduces metabolic responsiveness more than either one alone. The subsequent article by Homburger (6) adds the additional point that patients with cancer appear to demonstrate metabolic responses generally similar to the normal if they are in normal or near-normal nutritional condition.

Roche and Thorn (7) describe the use of the eosinophile test and the ACTH response in relation to surgery. This work has been published elsewhere (*New England J. Med.*, 242: 307, 1950) and will not be reviewed here in detail. The salient points are as follows:

First, the normal individual not suffering from allergy shows an eosinophile count of from 150 to 1500 cells per cubic millimeter. Following surgery this count drops 90 to 100 per cent, usually to levels from 30 to 0. This response with a return to normal or supernormal eosinophile count in the next few days constitutes the normal adrenal response to the stress of surgery. The initial eosinophile drop occurs after a transient rise (lasting 30 minutes) and then drops, reaching its lowest point 6 to 12 hours after the operation. There is evidence that in some cases a drop may commence prior to surgery with nervousness and apprehension.

Secondly, the response of the patient to ACTH, normal before surgery, does not return to normal until about the third or sixth day postoperatively, as judged by the eosinophile test. The reason for this relates merely to the fact that the surgical operation has in itself lowered the patient's eosinophile count to a level below which additional ACTH cannot lower it.

Thirdly, the finding of a normal or high eosinophile count during the immediate postoperative period points to the diagnosis of adrenal insufficiency. This adrenal insufficiency may be due to destruction of the adrenals themselves, as in Addison's disease, or functional adrenal insufficiency due to disorders in the pituitary, hypothalamus or thyroid. Such insufficiency may not have been recognized preoperatively and may be associated with postoperative lowering of the blood pressure and a shock-like state from which the patient is difficult to arouse. Preoperative identification of such patients may be accomplished by diminished eosinopenic response to ACTH or epinephrine.

This work, then, outlines the normal adrenal response to stress, its identification pre- and postoperatively, and intimates that the most clearcut interruptions of this response are found in deep-seated endocrine disturbances. Age, debility, obesity, heart disease, liver disease and all the other conditions which have been termed "poor operative risk" do not, alone, affect the eosinophile response to ACTH, epinephrine or stress.

BOOK REVIEW

In the discussion of this paper it is pointed out that the postoperative potassium and nitrogen losses are not well correlated and that the electrolyte changes are more characteristic of an ACTH-like response whereas the nitrogen loss may be related in large part to caloric deficit. This will strike a responsive note in the many surgical laboratories which have brought together evidence that caloric starvation greatly accentuates nitrogen negativity.

The article by Browne (10) should command the attention of any surgeon interested in protein metabolism. It is one of the most interesting in the book, especially when taken together with the important studies of Parson in the discussion and the subsequent addendum by Browne. This article is a description of the protein response to stress, both as surgical stress itself and as surgical stress studied in the light of the ACTH response. A true increase in nitrogen excretion is much more regularly produced by trauma than it is by the administration of ACTH. The variability between patients, according to degrees of debility, is nicely brought out, emphasizing the point that extensive pre-existent debility alters the nitrogen excretion phase possibly by the mechanism of reducing the amount of "labile" nitrogen. The discussion of Parson is based on his studies with tagged amino acids and demonstrates that an individual on a high protein diet "rejects" a high fraction of the tagged molecules fed. This "rejection" is imitated when ACTH is given to a person on a normal diet, demonstrating the nature of the shift in nitrogen metabolism produced by ACTH. In the discussion after this paper Doctor Browne contemplates the survival significance of the metabolic disorder following surgery; as he states, his remarks should lead to further work and cannot be regarded as dogmatic. They describe a very intriguing teleology to account for the increased excretion of nitrogen after stress. This theory can be summarized as follows: after trauma, the adrenal "loosens" body protein to make protein available for the healing of the wound. Since this protein is freed from its normal intracellular position, a greater amount is available for metabolic turnover, resulting in deamination and excretion of nitrogen in the urine. After a period of four to seven days of "loose" protein, the patient passes into convalescence and the protein is "tightened up" again in its intracellular position, the wound having healed. If the protein has previously been "loosened" or lost so that it cannot be made available again, wound healing may be interfered with; similarly if the patient has passed into the convalescent phase of positive balance and is again wounded, there may be a different response. It has been apparent for some time that the loss of nitrogen after trauma is in general correlated with a good convalescence and that efforts to reverse this response artificially are ill-conceived. It is therefore gratifying to read over these remarks by a worker who has been engaged in detailed study of these phenomena for over a decade.

Hume (11) describes, in dogs, the surgical lesion in the hypothalamus which is capable of blocking the eosinopenic response to stress. This is interpreted as demonstrating a center which connects the afferent nervous pathways from wound or injury to the endocrine axis of the pituitary-adrenal response to stress. The observation by Doctor Hume that small electrosurgical lesions here will block the whole complex, known as the "alarm reaction," is of very fundamental interest. It should be emphasized that the lesions described by Doctor Hume are very tiny, that they have all been made in dogs, and that their exact location is proved after sacrifice of the animal by serial section of the hypothalamus. Larger lesions, made more crudely or in other species, or unproved anatomically, cannot be considered to cast any light on the exact location of this center. It was also shown that electrical stimulation of this hypothalamic area produces a typical ACTH response. Cutting afferent nerves from the hind limb prevented the development of an adrenal response following surgical trauma to the limb. These two observations lend strength to the concept that the hypothalamic center may be the junction point of nervous and endocrine pathways in this response.

The articles by Pearson (25), Farber (26), and Taylor (27) deal with the treatment of various types of cancer with ACTH. In lymphatic malignancy a partial clinical

remission may occasionally be produced; this is particularly true if the leukemia is acute. Of greater interest to surgeons is the discouraging fact that the very few cases of carcinoma (and other epithelial tumors) which have been treated were disappointing. General feelings of well being and euphoria often go with ACTH treatment. These may progress to actual hysterical and maniacal tendencies after 14 to 21 days. They, of course, produce striking changes in the superficial clinical appearances of the cancer patient without altering the disease process.

The article by Sprague (29) is of exceptional interest because of the observation of hypokaliemic alkalosis in patients treated with ACTH. In order to make this observation, he carried out serial determinations of plasma bicarbonate, potassium and sodium during therapy. These workers have made more complete observations than others, in these regards. Those many surgeons who have been interested in the combination of extremely severe clinical illness with oliguria, a normal sodium, with a low chloride, a high bicarbonate, low plasma potassium and nitrogen retention will recall that this syndrome (which has been called "hypokaliemic alkalosis") is most commonly observed after intestinal obstruction, pyloric obstruction or diarrheal diseases, particularly when these situations have been compounded by trauma or operation. It is a commonplace observation that surgical operation produces a slight tendency in this direction which has erroneously been termed "potassium deficiency." This tendency after surgery is now seen to be but another result of adrenal cortical response. In addition, the full blown picture of severe hypokaliemic alkalosis may be hypothecated as the cumulative result of two conditions as follows:

1. Continued severe chloride loss, producing metabolic alkalosis.
2. Acute trauma, stress or operation, producing hypokaliemia as a by-product of adrenal activity.

When these two co-exist, the full picture of hypokaliemic alkalosis is produced, a clinical picture dramatically improved (if not relieved) by the administration of potassium salts parenterally. The importance of Sprague's paper lies in the fact that his patients after only four to seven days of ACTH frequently show a drop in plasma potassium, rise in CO_2 , and in some cases a fall in chloride.

The article by Bauer (38) tells of two patients with ulcerative colitis treated with ACTH. Clinical improvement was not dramatic, and side-effects, such as the development of a Cushing's-like picture, along with potassium loss, were pronounced.

The article by Stokes (42) describes the effect of ACTH on chronic liver disease. The surgeon pricks up his ears with interest, thinking of his many patients with parenchymatous liver disease who must undergo extensive abdominal surgery. His ears can go back down again. The agent is only effective—on the scanty knowledge available to date—in those patients where the liver disease is predominantly virus in origin.

The book taken together, particularly the first half, contains much general metabolic information of interest to surgeons. The specific use of the eosinophile test in relation to surgery is described, but more important than this is the general knowledge and understanding of the normal response to stress. There is much in the book that is incomplete, confusing and conflicting. This of course arises from its publication in the form of what might be called a "nation-wide preliminary report on ACTH."

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EDITORIAL ADDRESS

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